HIGHLY CONFIDENTIAL: SUBJECT TO PROTECTIVE ORDER

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION *County of Summit, Ohio, et al.* v. *Purdue Pharma L.P., et al.* *The County of Cuyahoga* v. *Purdue Pharma L.P., et al.*	CASE NO. 1:17-MD-2804 JUDGE POLSTER TRACK ONE CASES

EXPERT REPORT OF PROFESSOR MARGARET K. KYLE

May 10, 2019

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I. Introduction

I.A. Qualifications

(1) I am employed at the Ecole des Mines in Paris, a "grande ecole" that is a top engineering school in France.[1] I hold the chair in Markets for Technology and Intellectual Property and am a Professor of Economics.

(2) I received my BS in Policy Analysis from Cornell University and my PhD in Economics from the Massachusetts Institute of Technology. Prior to joining the faculty at the Ecole des Mines, I was a professor at Toulouse School of Economics, London Business School, the Fuqua School of Business at Duke University, and the Tepper School of Business at Carnegie Mellon University. I have also been a visiting professor at Northwestern's Kellogg School of Management and the University of Hong Kong, and a visiting scholar at the Federal Reserve Bank of San Francisco.

(3) I have taught undergraduate and graduate courses in microeconomics, health economics, innovation economics, and business strategy. I direct the PhD program and the undergraduate major in economics at Ecole des Mines. In addition, I have taught specialized courses for MBAs and other graduate students on the economics of the pharmaceutical industry at Duke, Northwestern, the University of Basel, and the University of Lausanne.

(4) I have been researching topics related to pharmaceutical innovation, marketing, and regulation for almost 20 years. My work has been funded by the World Health Organization, the World Trade Organization, the World Intellectual Property Organization, the European Commission, and the French National Research Agency, among other sources. I am a Research Fellow of the Centre for Economic and Policy Research and a member of the French government's National Council on Productivity. I am an associate editor of the International Journal of Industrial Organization, and a referee for many journals in economics and health policy. These tasks involve reviewing articles submitted to journals and evaluating whether they meet the standards of good economic and health care research and analysis. I have authored over 20 peer-reviewed publications in economics, management, and health policy, as well as more than 20 book chapters, reports, or articles intended for a policy audience. I regularly speak at conferences in the US and in Europe on topics related to pricing, innovation, and regulation of pharmaceuticals. I was recently named among the top "40 in

[1] Louis Heidsieck, "Classement des écoles d'ingénieurs: le surprenant palmarès de l'Usine nouvelle," Le Figaro.fr étudiant, February 6, 2019, available at https://etudiant.lefigaro.fr/article/classement-des-ecoles-d-ingenieurs-le-surprenant-palmares-de-l-usine-nouvelle_a9dfbf24-29fb-11e9-9279-a223b4194805/.

their 40s" of women working in competition policy.[2] My curriculum vitae is attached to this report in Appendix A.

I.B. Scope of charge and materials considered

(5) I have been asked by counsel for defendant Allergan to determine whether and to what extent Allergan's promotion of its prescription opioid products caused harm to Plaintiffs Cuyahoga and Summit counties.[3] I have also been asked to evaluate the opinions offered by Plaintiffs' experts Professors Gruber, Rosenthal, Cutler, and McGuire.

(6) I have also been asked to review the expert reports of Dr. Craig McCann and Ms. Lacey Keller to evaluate whether they have correctly identified transactions associated with Allergan products. Based on my review of the materials Dr. McCann provided on April 15, it appears that he is inappropriately assigning transactions to both Actavis and to Allergan, which results in duplicating those attributed to Allergan.[4] As of the date of this report, I have been unable to completely replicate Dr. McCann's analysis because of the late production of his backup materials. In particular, Dr. McCann's materials were not produced by Plaintiffs' counsel with his report, and his materials were still being provided as late as May 6. I am still assessing whether the provided backup materials are complete. Thus, I reserve the right to issue a supplement with this analysis. Based on my review of Ms. Keller's report, she does not attribute to Allergan any transactions that exceed the compliance metrics used in her report. In the event that Ms. Keller supplements her report at a later date and this conclusion changes, I reserve the right to supplement my report to address these new allegations.

(7) In reaching my opinions in this matter, I considered a variety of publicly available materials, as well as nonpublic materials made available to me through counsel. A complete list of the materials that I considered is provided in Appendix B. The materials I considered in forming my opinions contain facts and data that experts in my field (i.e., economists) would reasonably rely on in forming an opinion on the subject matter of this report.

(8) I reserve the right to update my opinions if new information or materials become available during the course of this litigation. If I am called upon to testify at trial, I also reserve the right to employ

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2 Women AT, 40 in their 40s: Notable Women Competition Professionals," accessed May 10, 2019, https://www.womenat.com/w-at-competition-40-in-their-40s

3 As I describe in Section II.B., Allergan has a complicated corporate history involving several acquisitions, sales, and other transactions. Unless otherwise specified, I describe activity by legacy companies Actavis and Watson as activity by "Allergan" to the extent it pertains to branded products currently owned by Allergan.

4 While I continue to explore Dr. McCann's recently produced backup materials, I note that his "Manufacturer NDC.do" program explicitly references this duplication issue in a comment that reads, "I do this in case an NDC belongs to both Actavis and Allergan." Following that comment, the duplication issue is executed on lines 998–999 which read:

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expand 2 if _merge==3 & Manufacturer=="Actavis", gen(new_f)
replace Manufacturer="Allergan" if new_f.
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demonstrative exhibits that summarize facts or opinions that are disclosed in this report, in my backup materials, or in new information that subsequently becomes available.

(9) I am being compensated for my time in this matter at a rate of 650 euros per hour. None of my compensation is contingent upon the outcome of this litigation.

I.C. Allegations

(10) Plaintiffs Cuyahoga and Summit counties, Ohio, allege that Defendants, certain manufacturers and distributors of prescription opioids, caused a significant increase in opioid abuse by intentionally (1) developing and executing a false and misleading marketing strategy beginning in the 1990s that knowingly misrepresented the risks and benefits of using prescription opioids for the treatment of chronic pain, and (2) evading restrictions on the distribution of prescription opioids.[5]

(11) With respect to the challenged marketing of prescription opioids, Plaintiffs allege that Manufacturer Defendants disseminated nine categories of misrepresentations concerning prescription opioids collectively, although Plaintiffs recognize that each Manufacturer Defendant did not disseminate alleged misrepresentations in all categories: (1) the risk of addiction from use of prescription opioids for chronic pain is low; (2) such risk can be easily identified and managed; (3) signs of addiction are "pseudoaddiction," requiring more prescription opioids; (4) withdrawal can be avoided by tapering; (5) dosage can be increased without additional risks; (6) long-term use of prescription opioids improves functioning; (7) alternative forms of pain relief are riskier; (8) OxyContin provides twelve hours of pain relief; and, (9) new formulas of certain prescription opioids successfully deter abuse.[6]

(12) Plaintiffs allege, often without regard to specific manufacturers and rarely with respect to Allergan, that Manufacturer Defendants:

- funded and controlled advocacy groups (which Plaintiffs label as "front groups"), certain doctors (whom Plaintiffs label as "key opinion leaders"), and professional education programs for doctors (which Plaintiffs refer to as "continuing medical education" courses or "CMEs") that they used to distribute patient education materials, treatment guidelines, medical research, and popular literature that overstated the benefits of opioids for chronic pain treatment while understating the risks of addiction;[7]

[5] Third Amended Complaint, County of Summit v. Purdue Pharma, MDL No. 2804, Case No. 17-md-2804 (N.D.Ohio Mar. 21, 2019.) [hereinafter "Summit 3AC"] ¶ 9; Cuyahoga 2AC at ¶ 9.

[6] Summit 3AC ¶ 172; Cuyahoga 2AC at ¶ 146.

[7] Summit 3AC ¶¶ 346-436; Cuyahoga 2AC at ¶¶ 320-410.

- advertised their branded prescription opioids in medical journals that touted the benefit of their respective products;[8]
- engaged in "unbranded advertising," which promoted the benefits of prescription opioids without specifically naming a particular brand-name product, thereby expanding the overall acceptance of prescription opioids for the treatment of chronic pain;[9]
- commissioned, edited, and distributed scientific articles and other ostensibly neutral publications that understated the risk and overstated the benefits of long-term opioid use[10];
- used sales representatives (whom Plaintiffs refer to as "detailers") to promote directly to individual prescribers their prescription opioids using misrepresentations, thereby allaying the targeted prescribers' concerns about prescribing prescription opioids for chronic pain;[11] and
- paid certain doctors to serve on their "speakers' bureaus," programs put on for other doctors.[12]

(13) Plaintiffs allege that Allergan:

- Promoted its two branded opioids—Kadian and Norco —"as formulated to be less addictive or less subject to abuse than other opioids;"[13]
- Made misrepresentations in a document titled "Learn More about customized pain control with Kadian;"[14] a salesforce training manual;[15] various market research studies concerning Kadian;[16] and a prescriber guide for Kadian;[17]
- Made misrepresentations regarding Kadian's ability to improve functioning and quality of life; and based on these alleged misrepresentations, the FDA issued a warning letter to Allergan on February 18, 2010;[18] and

8 Summit 3AC ¶¶ 437-438; Cuyahoga 2AC at ¶¶ 411-412.

9 Summit 3AC ¶¶ 439-440; Cuyahoga 2AC at ¶¶ 413-414.

10 Summit 3AC ¶¶ 441-446; Cuyahoga 2AC at ¶¶ 415-420.

11 Summit 3AC ¶¶ 447-456; Cuyahoga 2AC at ¶¶ 421-430.

12 Summit 3AC ¶¶ 457-459; Cuyahoga 2AC at ¶¶ 431-433.

13 Summit 3AC ¶ 66;

Second Amended Corrected Complaint, County of Cuyahoga v. Purdue Pharma, MDL No. 2804, Case No. 17-md-2804 (N.D.Ohio Mar. 25, 2018.) [hereinafter "Cuyahoga 2AC"] ¶ 45, 277.

14 Summit 3AC ¶ 219; Cuyahoga 2AC at ¶ 193.

15 Summit 3AC ¶ 220; Cuyahoga 2AC at ¶ 194.

16 Summit 3AC ¶ 221; Cuyahoga 2AC at ¶ 195.

17 Summit 3AC ¶¶ 222, 340; Cuyahoga 2AC at ¶¶ 196, 314.

18 Summit 3AC ¶ 276 fn 55; Cuyahoga 2AC at ¶ 250 n. 86.

- Made numerous payments to physicians nationwide, ostensibly for activities including participating on speakers' bureaus, providing consulting services, assisting in post-marketing safety surveillance and other services."[19]

(14) With respect to the challenged practices regarding the distribution of prescription opioids, Plaintiffs allege that Distributor Defendants (wholesale distributors of prescription medications) and Pharmacy Defendants (retail pharmacies that dispensed prescription opioids), together with Manufacturer Defendants, failed to control the supply chain, prevent diversion, report suspicious orders, and halt shipments of prescription opioids, as they are required to do under various legal and regulatory requirements, including the Controlled Substances Act.

(15) Plaintiffs also allege that Defendants:

- worked together to maintain artificially high DEA Quotas to ensure that suspicious orders were not reported to the DEA;
- failed to identify, investigate and report suspicious orders to the DEA when they became aware of such orders through various forms of data they possessed; and
- failed to report prolific prescribers of prescription opioids.

I.D. Summary of Plaintiffs' economic expert opinions[20]

(16) Professors Rosenthal and Cutler purport to offer a "general framework used to estimate harms caused by opioid shipments that resulted from defendants' misconduct. This framework requires three component calculations:

- The percentage of harms that is attributable to opioids;
- The percentage of opioid-related harms that is attributable to shipments of prescriptions;
- The percentage of shipment-related harms that is attributable to defendants' misconduct."[21]

(17) Professor Cutler employs regression analysis and claims to identify the percentage of harms to certain county departments that is attributable to opioids.[22] He then estimates the percentage of those opioid harms caused by increased opioid shipments based on the extent to which opioid shipments explain

[19] Cuyahoga 2AC at ¶ 46.

[20] Throughout this report, I use "Plaintiffs' economic experts" to refer to Professors Gruber, Rosenthal, Cutler, and McGuire.

[21] Expert Report of Professor David Cutler, March 25, 2019 [hereinafter "Cutler Rep."] ¶ 21.

[22] Cutler Rep. ¶ 8.

county-level variation in opioid-related mortality.[23] Professor Cutler does not connect any harms to Allergan or determine whether any conduct by Allergan caused the purported harms he identified in Cuyahoga and Summit counties; indeed, he testified that he does not connect any harms to any particular opioid products, nor does he assess whether conduct associated with any particular product, manufacturer, type of defendant, or even all defendants caused the opioid-related harms he purportedly identified in Cuyahoga and Summit counties.[24]

(18) Professor Rosenthal separately employs her own regression analysis—outside the context of Professor Cutler's model—to estimate the percentage of harms attributable to Defendants' collective misconduct. To do so, Professor Rosenthal assumes at the direction of Plaintiffs' counsel that all defendant manufacturer promotion beginning in 1995 was unlawful.[25] In her direct regression model, she uses manufacturer detailing visits to prescribers as a proxy for a wide variety of promotional efforts, and she assesses the extent to which changes over time in total sales of prescription opioid MMEs are explained by the "stock" of aggregate detailing that appreciates continually over time at a rate of about 8% annually.[26] Professor Rosenthal (or any other plaintiff expert for that matter) does not directly analyze the extent to which manufacturer detailing explains the county-level variation in mortality explored by Professor Cutler. Professor Rosenthal also does not assess how the detailing efforts of manufacturers differ from one another or how a manufacturer's efforts vary between products or over time, nor does she assess how the detailing efforts of any particular manufacturer compare to the other types of promotion undertaken by that manufacturer, such as hosting speaker bureaus, sponsoring key opinion leaders ("KOLs"), and funding so-called "front groups."

(19) Professor Cutler relies upon Professor Rosenthal's analysis to estimate the percentage of activity in certain divisions operated by Plaintiffs Cuyahoga and Summit counties that he asserts were caused by opioid shipments resulting from Defendants' misconduct. Professor Cutler testified that his final estimate of harm is dependent on Professor Rosenthal's estimate, and that if she were to conclude "that none of the shipments were associated with misconduct, then the outcome of [his] model would be no damages, no harms at all."[27] In Figure 1 and Figure 2, I list these percentages for each of the divisions in Cuyahoga and Summit County, respectively.

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23 Cutler Rep. ¶ 9.

24 Deposition of David Cutler, April 26, 2019 [hereinafter "Cutler April 26 Dep."] at 55–61.

25 Expert Report of Professor Meredith Rosenthal, March 25, 2019 [hereinafter "Rosenthal Rep."] ¶ 75.

26 In her preferred model, Professor Rosenthal calculates a monthly depreciation rate on the stock of detailing of -0.0067. This equates to 8% annual *growth* in her detailing stock. Rosenthal Rep. ¶ 72.

27 Cutler April 26 Dep. at 171:14–17.

Figure 1: Percentages of activity in certain Cuyahoga County divisions that was caused by opioid shipments that resulted from Defendants' misconduct, as estimated by Professors Rosenthal and Cutler

County division	Range of percentages over the period 2006–2018	
	Approach 1	Approach 2
ADAMHS Board	0.7%–6.7%	1.2%–6.7%
DCFS	1.0%–7.5%	1.6%–7.6%
Office of Prosecutor	1.2%–5.2%	2.0%–5.3%
Office of Public Defender	1.2%–5.2%	2.0%–5.3%
Court of Common Pleas	1.2%–5.8%	2.0%–5.9%
Juvenile Court	0.3%–2.1%	0.6%–2.1%
Sheriff's Office	1.2%–5.2%	2.0%–5.3%
County Jail	1.2%–5.2%	2.0%–5.3%
Office of Medical Examiner	1.9%–18.3%	3.2%–18.5%

Source:Cutler Rep. Table III.16A.

Figure 2: Percentages of activity in certain Summit County divisions that was caused by opioid shipments that resulted from Defendants' misconduct, as estimated by Professors Rosenthal and Cutler

County division	Range of percentages over the period 2006–2018	
	Approach 1	Approach 2
ADM Board	0.4%–7.3%	0.6%–7.4%
Children Services Board	0.9%–14.5%	1.6%–14.6%
Prosecutor	1.1%–5.6%	1.9%–5.7%
Court of Common Pleas	1.1%–5.6%	1.9%–5.7%
Juvenile Court	0.6%–3.2%	0.9%–3.3%
Sheriff's Office	1.1%–5.6%	1.9%–5.7%
County Jail	1.2%–4.5%	2.0%–4.5%
Alternative Corrections	1.2%–4.5%	2.0%–4.5%
Adult Probation	1.1%–5.6%	1.9%–5.7%
Medical Examiner	2.2%–17.7%	3.7%–17.8%

Source:Cutler Rep. Table III.16A.

(20) Professor McGuire's analysis is the final piece of the "damages" analysis constructed by Professors Cutler and Rosenthal. He explains that his analysis:

> [I]s based on a straightforward chain of reasoning that links (i) misrepresentations by manufacturer defendants and failure to detect and prevent excessive opioid shipments by all registrants of the Controlled Substances Act ('CSA'), including the distributor defendants, to greater shipments of prescription opioids; (ii) increases in prescription opioid shipments to increase in harms (e.g., crime, overdoses) in the Bellwether jurisdictions; and (iii) increases in harms to costs faced by Bellwether governments which devoted resources to contend with these harms.[28]

[28] Expert Report of Professor Thomas McGuire Damages to Bellwethers, March 25, 2019 [hereinafter "McGuire Damages Rep."] ¶ 8.

Specifically, Professor McGuire purports to, "reliably estimate past costs for the Bellwether governments that were affected by the opioid epidemic… that are 'variable' in that they could move up or down as the composition of services provided by each relevant division changes."[29] He then estimates damages "by applying the estimates of the percent of harms attributable to defendants' misconduct presented in the Cutler report (including both Approach 1 and Approach 2) to the identified affected costs in each division."[30] Professor McGuire calculates damages ranging from $125.5 million–$145.0 million for Cuyahoga County and from $68.8 million–$78.4 million for Summit County under two approaches applied during the period 2006–2018. He also estimates damages associated with the "public nuisance" allegedly caused by the Defendants to be approximately $20 billion. Professor McGuire makes no attempt to attribute his damage estimates by defendant or even type of defendant (i.e., manufacturer or distributor).

(21) Professor Gruber's opinions do not contribute directly to the Rosenthal-Cutler-McGuire causation and damages analysis. Rather, Professor Gruber:

- "Provides an empirical overview of the opioid crisis, including an evaluation of how the crisis evolved from one involving prescription opioids to one involving both prescription and illicit opioids;"[31]
- Explores the relationship between opioid shipments and mortality for large counties;[32]
- Describes how the reduced prescription opioid supply caused a transition to illicit opioids; and
- Explores the relationship between prescription opioid shipments and crime for large counties.[33]

(22) In Appendix C, I provide additional detail on the methodologies and opinions of Plaintiffs' economic experts.

I.E. Summary of opinions

(23) The causation and damage models offered by Plaintiffs' economic experts suffer from fatal technical and conceptual flaws that undermine any purported link between Plaintiffs' alleged damages and the manufacturer misconduct they allege, let alone any alleged Allergan misconduct. For example, Professor Rosenthal's model suffers from stationarity and other technical issues that lead to spurious results—results that fail to demonstrate any causal relationship. Because Professor Rosenthal's model provides the *critical input* that allows Professors Cutler and McGuire to link harms and damages to

[29] McGuire Damages Rep. ¶10.

[30] McGuire Damages Rep. ¶11.

[31] Expert Report of Professor Jonathan Gruber, March 25, 2019 [hereinafter "Gruber Rep."] ¶ 19.

[32] *See* Gruber Rep. ¶ 19.

[33] *See* Gruber Rep. ¶ 19.

alleged manufacturer misconduct, the conclusions of Professors Cutler and McGuire are baseless with respect to manufacturers given the fatal flaws in Professor Rosenthal's model. Moreover, their models are flawed in their own right.

(24) With respect to Allergan, Plaintiffs' economic experts concede they do nothing to assess whether Allergan's promotion was unlawful or contributed to their alleged damages. Professor Rosenthal's analysis assesses only the relationship between aggregate promotion and aggregate MMEs; it does not even attempt to assess whether Allergan's promotion expanded opioid MMEs. Professors Cutler and McGuire rely entirely on Professor Rosenthal's analysis to link opioid shipments and mortality to manufacturer promotion and fail to assess whether Allergan's promotion caused any harms. The analyses I describe in this report demonstrate that Allergan's promotion was limited in scope and magnitude, which is corroborated by its extremely small share of all opioid MMEs; did not cause an expansion in opioid MMEs; and does not explain the county-level variation in opioid shipments and opioid-related mortality analyzed by Professor Cutler.

(25) Plaintiffs' economic experts rely on flawed causation and damage methodologies that purport to calculate the harm resulting from the "combined effect of the Defendant manufacturers' promotion" by assuming that (1) all defendant promotion is unlawful (based upon counsel instruction) and (2) all defendant promotion had the same effects on prescribing (based upon the construction of Professor Rosenthal's model).[34] Professor Rosenthal concedes that her model does not separately assess the extent to which Allergan or any other manufacturer's conduct specifically expanded opioid MMEs.

> Q. What if a manufacturer engages only in limited detailing and not other types of promotional activities? It would not be conservative for that manufacturer to only look at detailing, correct?
>
> A. The purpose of my analysis is not to assign liability to individual defendants. It's to look at the aggregate effect. So I don't know what would be appropriate. That to me seems like a legal question.[35]

(26) By assigning the average aggregate detailing effect to Allergan, Professor Rosenthal ignores that the depreciated stock of Allergan detailing as captured by her model contributes almost nothing to her aggregate depreciated detailing stock, and she ignores that the types of promotion Allergan employed were much more limited than the types that she and other Plaintiff experts describe. Nearly all of the documents Plaintiffs or their experts identify with respect to Allergan promotion relate to Kadian, but Allergan's Kadian detailing was far more limited than the Alpharma Kadian detailing that preceded

[34] Professor Rosenthal's model makes this assumption despite numerous studies cited in IV.C. of her report that demonstrate otherwise. *See, e.g.*, Rosenthal Report ¶ 33 ("Berndt, et al. distinguish between 'industry expanding' and 'rivalrous' marketing efforts").

[35] Deposition of Professor Meredith Rosenthal, May 4, 2019 [hereinafter "Rosenthal May 4 Dep."] at 193:20–194:5.

it,[36] and most of Allergan's detailing occurred with agreement from the FDA. Plaintiffs' economic experts ignore these factors and have no basis on which to argue that Allergan's promotion was unlawful, and their models are incapable of distinguishing between the effects of Allergan's relatively limited promotion and any other promotion, lawful or not. I describe this opinion in Section III.

(27) The causation and damages approach offered by Plaintiffs' economic experts purportedly assesses the extent to which increases in aggregate manufacturer detailing resulted in *additional* prescribing, and do not assess the extent to which manufacturer detailing instead resulted in *substitution*. Professor Rosenthal explained this in her deposition:

> Q. Does your model account for rivalrous marketing?
>
> …
>
> A. The aggregate model that I put forth is intended to essentially obscure the rivalrous marketing, so to the extent that marketing only moves people from hydrocodone to oxycodone or the other direction, whatever it is, that will show up as a noneffect in my model. So I'm only looking at market expansion because the question I care about is market expansion.[37]

While Professor Rosenthal claims that rivalrous marketing would show up as a "noneffect" in her model, the reality is that she applies the average effect of detailing to every manufacturer, regardless of whether all of their marketing was rivalrous or none of it was. Because Professor Rosenthal's approach assumes that all detailing has the same incremental effect, it fails to consider whether some detailing (e.g., detailing associated with certain manufacturers or products) had no effect on total prescribing or resulted in prescribers switching from opioids they were already prescribing. In Section IV, I demonstrate that her aggregate approach ignores the rivalrous nature of Allergan's promotion and specific Allergan prescribing patterns that are inconsistent with the theory that Allergan's promotion expanded opioid prescribing.

(28) Kadian and Norco are not responsible for the increase in opioid MMEs that occurred over the period from 1997 through 2010. With respect to Cuyahoga and Summit counties, as well as nationally, the extremely low share and timing of MMEs associated with Allergan's prescription opioids are inconsistent with the notion that Allergan's promotion caused an overall increase in opioid prescribing. The notion that Allergan's promotion expanded prescribing is also inconsistent with deposition testimony and contemporaneous sales documents that reflect Allergan's objective to maintain prescription volume or substitute volume from competing products, rather than expand overall opioid prescribing. Using the available prescriber-level detailing and prescribing data on

[36] As I detail in Section II.B, Alpharma sold and marketed Kadian prior to Allergan acquiring Kadian in December 2008.

[37] Rosenthal May 4 Dep. at 206:10–206:25.

Kadian, I analyze whether prescribers who received detailing from Allergan expanded their Kadian prescribing after they were detailed by Allergan. I find that these prescribers routinely either maintained or reduced their level of Kadian prescribing. Using data from the Ohio Automated Reporting Rx Reporting System ("OARRS"), I also demonstrate that prescriber and patient-specific patterns of Kadian prescribing are consistent with rivalrous marketing and with providers exercising their clinical discretion.

(29) None of Plaintiffs' experts directly tests the links between promotion and shipments or promotion and harm at the county level, despite the availability of data that would allow them to have done so at least for particular products and defendants. Instead, Professor Rosenthal assesses the link between *national* opioid detailing and *national* opioid MMEs, which yields unreliable estimates about the extent to which county-level detailing caused county-level opioid prescribing, opioid shipments, or opioid-related harm. Professor Rosenthal's indirect model is her only attempt at examining county-level variation, in which she assumes (rather than tests) that all unexplained county-level variation in opioid shipments must be caused by manufacturer conduct. A direct assessment of this link reveals that Allergan county-level detailing does not explain county-level variation in opioid shipments or county-level opioid mortality. I describe this opinion in Section V.

(30) In Sections III–IV, I establish that Plaintiffs' economic experts have failed to demonstrate that any harm was caused by Allergan. In Section VI, I explain that the technical and conceptual flaws in Professor Rosenthal's models render them incapable of establishing a link between Allergan detailing and opioid MMEs. For example, Professor Rosenthal's preferred model suffers from a nonstationarity issue that renders her results spurious, and both her direct and indirect models omit important factors that likely explain variation in opioid MMEs. The findings of Professors Cutler and McGuire are therefore irrelevant, at least with respect to manufacturers, because they rely entirely on Professor Rosenthal flawed approach to connect harms to manufacturer promotion. I also explain the flaws in the analyses of Professors Cutler and Gruber that omit important factors that likely explain variation in opioid mortality, and demonstrate that Professor Cutler's model overstates the relationship between opioid prescribing and mortality. I also offer general criticisms of Professor McGuire's calculation of damages as well as his quantification of "public nuisance" that he purports to attribute to prescription opioids.

II. Background

II.A. Economics of pharmaceutical promotion

(31) In her report, Plaintiffs' expert Professor Rosenthal provides background on the pharmaceutical industry and the effects of pharmaceutical promotion generally. In this section, I provide additional context to her review of economic literature by describing how promotion differs in important ways across manufacturers and markets, and the importance of accounting for physician characteristics and other confounding factors when estimating the impact of promotion for prescription opioids.

(32) Within a class of products that address a disease or condition, pharmaceutical products are typically distinguished by both their active ingredient and branded status as well as their formulation and approved indication. Within the class of opioids, morphine sulfate and oxycodone are distinct chemicals that treat pain. Kadian is a branded version of morphine sulfate, and OxyContin is a branded version of oxycodone.

(33) Prescription medications of the same class have different chemical and clinical properties, which physicians may consider when choosing among them. For example, some opioids are short-acting, others are long-acting, and some have abuse-resistant formulations. Many opioids come in pill or capsule form, while others are transdermal patches, sublingual sprays, or intravenous administrations. These properties make them more or less suited to a particular patient's needs based upon the individual characteristics of each patient. In the language of economics, prescription medications with different active ingredients, formulations, strengths, and methods of delivery are differentiated products.

(34) Prescription medications usually have generic equivalents following the expiration of patent protection or exclusivity. These products do not have a brand name and are determined to be bioequivalent to the name brand, thus making them near-perfect substitutes for the branded product and other generic products with the same active ingredient. When a generic exists, state laws and commercial and government payors typically require that a pharmacist dispense a generic instead of the branded product. As a result, generics usually attain significant market share within a few years of market entry. For drugs that faced generic entry beginning in 2013–2014, for example, generics captured almost 90% of the market within 12 months.[38]

(35) Manufacturers typically promote their branded products only while they are still under patent protection, because sales of the branded product fall steeply following generic entry. Promotion serves two functions. First, promotional efforts can be an important source of clinical information for

[38] Henry Grabowski, Genia Long, Richard Mortimer and Ani Boyo, "Updated trends in US brand-name and generic drug competition," *Journal of Medical Economics* 19, no. 9 (2016), 840–843.

physicians about new therapies or new differentiated products within an existing therapeutic class. Second, promotion informs and reminds physicians of the existence of available products. This is important because physicians tend to have prescribing habits that cause them to continue to prescribe the same drugs they prescribed in the past, even if others may be more effective for certain patients.[39]

(36) Thus, promotion can expand the market (as advertising of the iPhone in 2007 likely expanded the market for smartphones) or cause substitution among products (as advertising of the iPhone in 2019 likely serves to maintain or increase Apple's share of smartphones relative to Android, but does not add many consumers who do not already own a smartphone). In pharmaceutical markets, early movers' promotional efforts are usually market expanding, while subsequent entrants focus on gaining share at the expense of incumbents. Majumdar et al. (2003) show that promotional efforts were more effective than the publication of articles alone in increasing physicians' adoption of new medical evidence, and Azoulay (2002) finds that "[t]he evidence suggests that comparative science constitutes a potent business-stealing weapon."[40]

(37) Promotion is not itself unlawful, and studies have established that lawful promotion can be market-expanding, and market expansion can increase patient welfare.[41] Indeed, Plaintiffs' expert Professor Perri acknowledges that pharmaceutical promotion serves the important purpose of providing information to doctors to keep "their drug knowledge and their disease knowledge" current.[42] At issue in this case is whether some promotion was unlawful, and if so, what incremental harm if any was caused by the unlawful promotion relative to what would have resulted from lawful promotion.

(38) While Professor Rosenthal cites studies on physician responses to a type of unlawful promotion, namely off-label use, these studies do not establish that unlawful and lawful promotion have identical effects on sales. In fact, Larkin et al. estimated a larger change in prescribing of on-label uses relative to off-label uses resulting from restrictions on detailing, although the authors did not design their study to address the question of whether on-label and off-label marketing efforts have differential impacts.[43] Recent work by Shapiro (2017) finds only a small effect of detailing on off-label

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39 Andrea Coscelli, "The Importance of Doctors' and Patients' Preferences in the Prescription Decision," The *Journal of Industrial Economics* 48, no. 3 (2000), 349–369;

Janakiraman et al., "Physicians' Persistence and Its Implications for Their Response to Promotion of Prescription Drugs," Management Science 54(6):1080-1093.

40 Azoulay, Pierre, "Do Pharmaceutical Sales Respond to Scientific Evidence," *Journal of Economics & Management Strategy*, 11, no. 4 (2002) at p. 576;

See Sumit R. Majumdar, Finlay A. McAlister, Stephen B. Soumerai, "Synergy between publication and promotion: comparing adoption of new evidence in Canada and the United States," *The American Journal of Medicine* 115, no. 6 (2003), 467–472.

41 For example, Professor Cutler demonstrates in his 2007 article published in Health Affairs that increasing the prescribing of antihypertensives would increase patient welfare. *See* Cutler et al (2007) The Value Of Antihypertensive Drugs: A Perspective On Medical Innovation.

42 Deposition of Matthew Perri, III, BS Pharm, Ph.D., Rph, April 23, 2019 [hereinafter "Perri Dep. 1/2"] at 111:17-111:23.

43 *See* Ian Larkin, Desmond Ang, Jerry Avorn, and Aaron S. Kesselheim, "Restrictions on Pharmaceutical Detailing Reduced Off-Label Prescribing of Antidepressants and Antipsychotics in Children," *Health Affairs* 33, no. 6 (2014),

prescriptions.[44] These results suggest that lawful and unlawful marketing may not have the same effects, but Professor Rosenthal neither tests her assumption that they do, nor offers any evidence from the literature that they do.

(39) While there is general agreement that pharmaceutical promotion increases sales, estimates of the elasticity of sales to promotion vary substantially across studies. In other words, while the academic literature agrees on the direction of the effect, there is less agreement about the magnitude, which is critical to the estimation of damages in this case. The lack of consensus is due to the use of different methodologies and the application to different market settings, as well as to the difficulty of distinguishing between the effect of promotion and other confounding factors that drive sales. Papers that use richer datasets, such as those at the physician-level over time, can better identify the causal effect of promotion than those that rely on aggregate data, as Professor Rosenthal does. For example:

- One example of such a paper, cited by Professor Rosenthal, is Mizik and Jacobson (2004).[45] They note that failure to control for physician-specific effects lead to biased estimates of the impact of detailing on sales. While they find a positive and significant effect of detailing on sales, the effect of detailing *diminishes* over time, and becomes indistinguishable from zero by six months after a detailing visit. In addition, the effect of detailing differs across the drugs they study. For the last entrant, the business substitution effect dominated the market expanding effect.
- A more recent paper that also uses physician-level data over time is Datta and Dave (2016), likewise cited by Professor Rosenthal.[46] While this study found a positive effect of detailing on sales, the authors noted that this "effect is substantially smaller than those in the literature based on aggregate information, suggesting that most of the observed relationship between physician-directed promotion and drug sales is driven by selection bias."[47] They also found that detailing in the drug market that was the focus of their study had *no* effect on class-level demand, i.e. it is purely business-substitution.
- Professor Rosenthal was a co-author on a study of how promotion affected the treatment of depression.[48] This study found "[p]romotion to physicians was not associated with either the

1014–1023.

44 Bradley T. Shapiro, "Informational Shocks, Off-Label Prescribing, and the Effects of Physician Detailing," *Management Science* 64, no. 12 (2018), 5930–44.

45 *See* Rosenthal Rep. ¶ 34;

See Natalie Mizik and Robert Jacobson, "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions, *Management Science* 50, no.12 (2004), 1704–1715.

46 *See* Rosenthal Rep. ¶ 34;

See Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics* 26 no. 4 (2016), 450–468.

47 Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics* 26 no. 4 (2016), 450.

48 *See also* Julie M. Donohue, Ernst R. Berndt, Meredith Rosenthal, Arnold M. Epstein, and Richard G. Frank, "Effects of Pharmaceutical Promotion on Adherence to the Treatment Guidelines for Depression," *Medical Care* 42, no. 12 (2004),

initiation of treatment with an antidepressant or with the duration of therapy," although physician characteristics did explain those outcomes.[49]

- Professor Rosenthal was the lead author of a study on the effects of both direct-to-consumer advertising and physician detailing in five therapeutic areas.[50] This study noted "substantial heterogeneity in…physician-oriented promotion to sales ratios."[51] In addition, the results for the effect of detailing on quantity sold were "neither robust nor precisely estimated."[52]

The results from these papers again underscore the importance not only of controlling for confounding factors (such as physician characteristics), but also the dubiousness of Professor Rosenthal's decision to apply the average effect of all detailing in aggregate to every manufacturer and product, regardless of the particular messaging or when in the product's life cycle it occurs. Indeed, Professor Rosenthal herself acknowledges the importance of understanding the timing of marketing in the product life cycle: "Estimates [of the elasticity of promotion] vary across studies, in part due to differences in the classes of drugs studied, the product lifecycle, time periods, and the research designs implemented."[53] Further, none of these studies finds that promotional efforts *appreciate* over time, in contrast to Professor Rosenthal's results. Professor Rosenthal acknowledged that she is not aware of any study that has a negative depreciation rate.[54]

(40) A large body of academic work has established that physician characteristics are important determinants of prescribing. In many cases, these characteristics are more important than detailing in explaining prescribing:

- Physicians are generally persistent in their prescribing behavior, and those physicians who are most persistent are the least sensitive to detailing.[55]

1176–1185.

49 Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics* 26 no. 4 (2016), 450.

50 Meredith B. Rosenthal, Ernst R. Berndt, Julie M. Donohue, "Demand Effects of Recent Changes in Prescription Drug Promotion," in Frontiers in Health Policy Research, Vol. 6, eds. David M. Cutler and Alan M. Garber, 1–26 (Cambridge, MA: The MIT Press, 2003).

51 Meredith B. Rosenthal et al., "Demand Effects of Recent Changes in Prescription Drug Promotion," in Frontiers in Health Policy Research, Vol. 6, eds. David M. Cutler and Alan M. Garber, (Cambridge, MA: The MIT Press, 2003), 10.

52 Meredith B. Rosenthal et al., "Demand Effects of Recent Changes in Prescription Drug Promotion," in Frontiers in Health Policy Research, Vol. 6, eds. David M. Cutler and Alan M. Garber, (Cambridge, MA: The MIT Press, 2003), 21.

53 *See e.g.*, Rosenthal Report, ¶ 32.

54 Rosenthal May 4 Dep. at 259:25–260:6.

55 Ramkumar Janakiraman, Shantanu Dutta, Catarina Sismeiro, and Phillip Stern, "Physicians' Persistence and Its Implications for Their Response to Promotion of Prescription Drugs," *Management Science* 54, no. 6 (2008), 1090.

- Berndt et al. (2015) estimate a model of physician learning-by-doing, i.e. through experience and personal observation of their patients' experiences. They conclude that their model explains prescribing patterns better than an alternative model based on promotional efforts.[56]
- Physicians are more sensitive to formulary placement of a product than they are to detailing and sampling.[57]
- Recent work focusing specifically on opioid prescribing finds that physician characteristics, in particular where a physician trained, are important in explaining patterns of prescribing.[58]

(41) These studies show that the effect of promotion differs in important ways across manufacturers and markets, and its estimated effect is lower when physician characteristics and other confounding factors are taken into account. As I explain later in this report, Plaintiffs' economic experts have ignored differences in promotion and the effects of confounding factors.

II.B. Allergan's corporate history, product portfolio, and opioid products

(42) Allergan is a leading developer and manufacturer of pharmaceutical, device, biologic, surgical, and regenerative medicine products for patients around the world. Allergan develops and markets a portfolio of products primarily for the central nervous system, eye care, medical aesthetics and dermatology, gastroenterology, women's health, urology, and anti-infective therapeutic categories. Allergan's 17 top-selling products include two types of Botox®, four eye care drugs, breast implants, a body contouring device, facial fillers, an oral contraceptive, and medicines to treat depression, schizophrenia, irritable syndrome, skin grafts, pancreatic insufficiency, hypertension, and ulcerative colitis (an inflammatory bowel disease). Allergan's two remaining opioid products are remnants from prior acquisitions, with no promotion occurring since 2013.

- **Kadian:** In December 2008, King Pharmaceuticals acquired Alpharma, Inc.[59] In order for the Federal Trade Commission to approve the merger, Alpharma was ordered to divest the rights to Kadian.[60] A former affiliate of Allergan, Actavis Elizabeth LLC, acquired Kadian (NDA 020616)

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56 *See* Berndt, Ernst, et.al., "The Heterogeneity of Concentrated Prescribing Behavior: Theory and Evidence from Antipsychotics," *Journal of Health Economics*, 40 (2015), 26–39.

57 Andrew J. Epstein and Jonathan D. Ketcham, "Information technology and agency in physicians' prescribing decisions," *RAND Journal of Economics* 45, no. 2 (2014), 422, 438–439.

58 Molly Schnell & Janet Currie, "Addressing the Opioid Epidemic: Is There a Role for Physician Education?," *American Journal of Health Economics* 4, no. 3 (2018), 404–407.

59 Reuters, "UPDATE 2-King Pharma to acquire Alpharma for about $1.6 bln," November 24, 2008, available at https://www.reuters.com/article/king-alpharma-idUSN2450242820081124.

60 Federal Trade Commission, "FTC Intervenes in King Pharmaceuticals Acquisition of Rival Alpharma Inc.," December 29, 2008, available at https://www.ftc.gov/news-events/press-releases/2008/12/ftc-intervenes-king-pharmaceuticals-acquisition-rival-alpharma.

via an Asset Purchase Agreement from King Pharmaceuticals on December 17, 2008.[61] I have been asked to assume that through this purchase, Actavis Elizabeth LLC did not assume liability for any conduct related to Kadian prior to the 2008 acquisition. Today, Allergan owns Kadian® but contracts with Teva Pharmaceuticals, Inc. to manufacture Kadian and contracts with UPS SCS, Inc. to distribute Kadian on its behalf.[62]

- **Norco:** A former affiliate of Allergan, Watson Laboratories, Inc., obtained approval for Norco in 1997.[63] Today, Allergan owns Norco but contracts with Teva Pharmaceuticals, Inc. to manufacture Norco and contracts with UPS SCS, Inc. to distribute Kadian on its behalf.[64]

(43) Professor Rosenthal attributes detailing to Allergan for "promotion contacts" associated with four other branded opioid products, but I understand that Allergan either divested those products (Lorcet), discontinued them (Combunox and Maxidone), or ceased participation in a joint marketing and sales agreement (Reprexain).[65] I have been asked by counsel to assume these products are not the subject of any allegations of marketing misconduct in this case, and therefore I have not included them in the analyses I describe in the body of this report. Nevertheless, I also ran alternative versions of my analyses that included these additional drugs and determined that they do not materially impact my analyses or conclusions. I include these analyses in my backup data. Below I summarize the history of these four products.

- **Combunox:** Actavis acquired Forest Laboratories, Inc. in July 2014. Prior to the acquisition, Forest Laboratories, Inc. sold Combunox, a product for which Forest received approval on November 26, 2004. There were a total of 51 Combunox prescriptions in Cuyahoga and Summit counties between 2008 and 2011. Combunox has been discontinued since December 2011.[66]
- **Maxidone:** On October 12, 2000, Watson Pharma, Inc. announced the addition of Maxidone to its product portfolio.[67] Throughout the time it was promoted by Watson Pharma, Inc., Maxidone

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61 Allergan_MDL_01514893 at -4893–4945.

62 ALLERGAN_MDL_03367042 at -7042-7046; 2015 UPS Allergan Contract ALLERGAN_MDL_01396729 at -6729-6749.

63 U.S. Food and Drug Administration, "Drugs@FDA: FDA Approved Drug Products: Norco," accessed May 8, 2019, available at https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=040099.

64 ALLERGAN_MDL_03367042 at -7042-7046; 2015 UPS Allergan Contract ALLERGAN_MDL_01396729 at -6729-6749.

65 Professor Rosenthal also attributes Anexsia to Allergan for at least part of the time period included in her analysis, but no Allergan affiliate ever sold Anexsia. Specifically, Anexsia was sold by Andrx pursuant to a licensing agreement with Mallinckrodt that was terminated prior to Allergan's acquisition of Andrx. Professor Rosenthal attributes an immaterial amount of Procet detailing to Allergan: 170 total contacts out of the 10.5 million contacts included in her analysis across all opioids. I understand that there is insufficient information to even determine if this drug was ever associated with Allergan or one of its affiliates, and I understand that Plaintiffs have not made any allegations specifically with respect to Procet. *See* Teva-Allergan MPA Schedules ALLERGAN_MDL_03367048 at -7048-7153; Rosenthal Rep. Table C.2.

66 *See* U.S. Food and Drug Administration, "Approved Drug Products with Therapeutic Equivalence Evaluations: 32nd Edition," 2012, available at http://data.nber.org/fda/orange-book/historical/1986-2016/1_orange_book_PDFs/full_books_1980-2016/2012.pdf.

67 *See* October 12, 2000 Product Introduction Notification ALLERGAN_MDL_02579713 at -9713.

was classified by the DEA as a Schedule III medicine. There were only 39 Maxidone prescriptions in Cuyahoga and Summit counties since 2006, and none after 2010. Maxidone was discontinued in February 2014.[68]

- **Reprexain:** Between 2004 and February 2007, Watson Pharmaceuticals, Inc., collaborated with Interpham, Inc. (the ANDA holder) in the marketing and sale of Reprexain.[69] During that time, Reprexain was labeled by the DEA as a Schedule III medicine. Amneal Pharmaceuticals NY LLC acquired Interpharm in 2008 and still owns Reprexain. Reprexain was rescheduled to Schedule II effective October 6, 2014.[70] There were only 402 Reprexain prescriptions in Cuyahoga and Summit counties between 2004 and February 2007.
- **Lorcet**: Allergan acquired Forest Laboratories, Inc. in July 2014. In February 2014, prior to and unrelated to Allergan's acquisition, Forest Laboratories, Inc. sold Lorcet and related assets to Libertas Pharma, Inc., a subsidiary of Mayne Pharmaceuticals. Mayne Pharmaceuticals still owns Lorcet today. I understand that Forest Laboratories promoted Lorcet for a brief period of time in the 1990s when Lorcet was labeled by the DEA as a Schedule III opioid. Lorcet was rescheduled to Schedule II effective October 6, 2014,[71] after Forest had sold the brand to Mayne. There were fewer than 1,000 Lorcet prescriptions in Cuyahoga and Summit counties since 2006.

II.C. Allergan's promotional efforts and the scope of Plaintiffs' allegations related specifically to Allergan

(44) In this section I describe the relatively limited scope of Allergan's promotion for Kadian and Norco, the substitution (not expansion) objective of Allergan's Kadian promotional efforts, and Allergan's corrective action response to an FDA warning letter regarding certain Kadian marketing materials. I am not aware of any allegations or evidence regarding Allergan's promotion of Norco other than the limited evidence described in the following section. Thus, my discussion of Allergan's promotion focuses almost entirely on Kadian.

68 *See* ALLERGAN_MDL_03435513.

69 June 07, 2004 Email & Press Release Announcing Launch ALLERGAN_MDL_01830938 at -0938-0939; ALLERGAN_MDL_01830941 at -0941-0944; June 14, 2006 Email Discussing No Longer Promoting Reprexain ALLERGAN_MDL_01728789 at -8789-8790.

70 Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II, 79 Fed. Reg. 49,661-01 (August 22, 2014) (to be codified at 21 C.F.R. pt. 1308).

71 Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II, 79 Fed. Reg. 49,661-01 (August 22, 2014) (to be codified at 21 C.F.R. pt. 1308).

II.C.1. The types of promotion Allergan employed were much more limited than the types described by Professor Rosenthal and other Plaintiff experts

(45) Professor Rosenthal and Plaintiffs' expert Professor Matthew Perri describe a wide variety of promotional activities undertaken by manufacturers of prescription opioids. These activities include:[72]

- "Visits or phone calls by pharmaceutical sales representatives to physicians (detailing)"
- "Free samples"
- "Sponsorship of medical education events," including "accredited CME and non-certified education"
- "'Transfers of value' to physicians (e.g., speaking fees, meals)"
- "Influencing treatment guidelines or algorithms"
- "Unbranded educational campaigns," or "unbranded marketing, including partnering with advocacy organizations such as the American Pain Foundation, American Pain Society, American Academy of Pain Medicine"
- "Research, publications & medical journal advertising"
- "Peer-to-peer marketing [using] key opinion leaders (KOLs) or 'influencers' and word-of-mouth"
  - "Industry advisory boards"
  - "Health advocacy groups"
- "Direct-to-consumer (DTC) advertising of prescription drugs on television, radio, and internet and in popular magazines"
- "Payor-oriented marketing…seeking to influence formulary placement"

(46) My understanding, informed by counsel and my review of documents, Plaintiffs' complaints, discovery responses, witness testimony, and expert reports, is that Allergan engaged in these activities to a much lesser degree compared to the other manufacturers, if at all. For example:

- I have not seen any evidence that Allergan influenced treatment guidelines. Indeed, Allergan did not manufacture or promote a branded extended-release long-acting opioid until it acquired Kadian in December 2008—approximately a decade after the alleged conspiracy to expand opioid prescribing began.[73]

[72] Rosenthal Rep. ¶ 23; Expert Report of Matthew Perri III, BS Pharm, PhD, RPh, March 25, 2019 [hereinafter "Perri Rep."] ¶ 36, 37, 39, 41, 46, 60.

[73] *See* Summit 3AC ¶ 4.

- In addition, I understand that Allergan did not host speaker bureaus for Kadian. Allergan's Business Rules for its salesforce state that "[a]t this time Actavis will not be participating in any Promotional Speaker Programs."[74] Emails during Allergan's promotion of Kadian likewise confirm that it did not conduct any speaker programs for Kadian. For example, on August 26, 2011, Nathalie Leitch (Actavis's project manager for Kadian) explained to Doug Boothe (Actavis's former CEO) that "[w]e have looked at speakers programs and every derivative thereof and have made the decision not to pursue."[75] Doug Boothe confirmed this point at his deposition.[76]
- With respect to key opinion leaders (KOLs), Doug Boothe confirmed at his deposition, "we at Actavis did no KOL activity for Kadian or any of our generic approved products."[77]
- I also have not seen any evidence that Allergan participated in Continuing Medical Education related to opioids. The same Business Rules disavowing Allergan's involvement with speaker bureaus likewise state, "[a]t this time Actavis will not be offering any Educational Grants."[78] Although Allergan did fund an educational website called "PainEDU.org" as part of its agreement with the FDA to provide a Risk Management Plan for Kadian, I understand Allergan had no editorial control over this website.[79]

(47) Professor Perri admitted that he did not believe Allergan ever "worked with pain advocacy organizations to promote opioids."[80] The documents Plaintiffs have cited to support the claim that Allergan worked with patient advocacy organizations and KOLs demonstrate that Allergan participated in these activities only in connection with the anticipated launch of a drug called "MoxDuo." However, MoxDuo was never approved, and thus was never promoted or detailed. The FDA rejected the new drug application for MoxDuo, as stated in a letter dated June 25, 2012.[81]

(48) Outside the MoxDuo context, Plaintiffs' experts cite a handful of documents that they claim show involvement with KOLs. Specifically, Schedule 18 of Professor Perri's report concerning payments to KOLs lists four documents showing payments related to Norco made to four doctors.[82] Professor Perri cites no evidence explaining the reason for these payments or describing what these doctors did

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74 ALLERGAN_MDL_01104711 at -4716.

75 ALLERGAN_MDL_00400518 at -0518-0520.

76 Deposition of Douglas Boothe, January 17, 2019 [hereinafter "Boothe Dep."] at 199:9–12.

77 Boothe Dep. at 363:23–364:7 (objections omitted); *See also* Deposition of Jennifer Altier, August 2, 2018 [hereinafter "Altier Dep."] at 369:10–13.

78 ALLERGAN_MDL_01104711 at -4717; *See also* Altier Dep. at 368:23–369:18.

79 ALLERGAN_MDL_01780378 at -0378-0379; ALLERGAN_MDL_01434355 at -4355-4360.

80 Deposition of Matthew Perri, III, BS Pharm, Ph.D., RPh, April 24, 2019 [hereinafter "Perri April 24 Dep."] at 606:13–20.

81 ALLERGAN_MDL_00165809 at -5809-5812.

82 Perri Rep. Schedule 18; *See also* ALLERGAN_MDL_03352425 at -2425-2426; ALLERGAN_MDL_03352878 at -2878-2879; ALLERGAN_MDL_03352423 at -2423-2424; ALLERGAN_MDL_03352880 at -2880-2882.

or did not say about Norco, and thus offers no evidence that these payments were unlawful.[83] The U.S. Department of Health and Human Services ("HHS") Office of the Inspector General ("OIG") acknowledged in its April 2003 "Compliance Program Guidance for Pharmaceutical Manufacturers" that grants paid to speakers may be appropriate under certain conditions.[84] The Pharmaceutical Research and Manufacturers of America ("PhRMA") published a "code on relationships with U.S. healthcare professionals" effective July 2002, and it updated the code effective January 2009. The PhRMA code also permits "speaker programs and speaker training meetings" under certain conditions.[85] The OIG states in its guidance that "the PhRMA Code…will substantially reduce the risk of fraud and abuse and help demonstrate a good faith effort to comply with the applicable federal health care program requirements."[86]

(49) Allergan promoted Kadian between 2009 and 2013 by detailing physicians. After the December 30, 2008 Kadian acquisition closed, Allergan did not initially plan to detail Kadian to doctors.[87] Only after Allergan discovered that other companies were telling prescribers and wholesalers that Kadian had been discontinued did Allergan decide that it might be worthwhile "to let physicians know that [the] product was still available."[88]

(50) The Kadian patent was set to expire in April 2010, which would invite generic entry, meaning that Kadian had a short remaining product life.[89] According to Actavis's CEO Doug Boothe, "[w]e had no aspirations that we were going to increase the scripts. We were trying to slow down the rate in which prescriptions stopped."[90] To that end, on May 1, 2009, Allergan hired a contract salesforce through Ventiv Commercial Services, LLC ("Ventiv") to detail Kadian to prescribers.[91] Allergan implemented a small, 18-member Kadian salesforce supervised by two managers called "regional business directors."[92] The salesforce's goal was "to let prescribers know that the product was available and to

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83 Perri April 24 Dep. at 600:1–25; 602:17–603:16; 605:7–18; 605:23–606:12 (objections omitted).

84 Office of Inspector General, U.S. Department of Health and Human Services, "Compliance Program Guidance for Pharmaceutical Manufacturers," April 2003, p. 21, available at https://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf.

85 PhRMA, "Code on Interactions with Healthcare Professionals," revised July 2008 and effective January 2009, pp. 3, 9–10, available at https://www.acpe-accredit.org/pdf/Code%20on%20Interactions%20HC%20Professionals.pdf.

86 Office of Inspector General, U.S. Department of Health and Human Services, "Compliance Program Guidance for Pharmaceutical Manufacturers," April 2003, p. 31, available at https://oig.hhs.gov/fraud/docs/complianceguidance/042803pharmacymfgnonfr.pdf.

87 ALLERGAN_MDL_01190060 at -0060.

88 Boothe Dep. at 175:8–176:4; Actavis "knew that Alpharma hadn't been talking about the product for a while, the reps hadn't been promoting Kadian" so Actavis's "main goal was just to make prescribers aware … that Kadian was available." *See* Deposition of Nathalie Leitch, January 22, 2019 [hereinafter "Leitch Dep."] at 44:20–45:14.

89 Leitch Dep. at 37:15–38:12.

90 Boothe Dep. at 176:5–177:8.

91 *See* Allergan's Fourth Amended Objections and Responses to Plaintiffs' Corrected Second Set of Interrogatories, *In re National Prescription Opiate Litigation*, MDL No. 2804, Case No. 17-md-2804 (N.D.Ohio Mar. 4, 2019.) pp. 35–38.

92 Boothe Dep. at 176:5–177:8, 323:10–325:11; Leitch Dep. at 40:17–41:5.

provide information about the product."[93] The contract salesforce's promotion was essentially an awareness campaign that attempted to stem the decline in Kadian prescribing.[94]

(51) At the outset of detailing, Allergan used marketing materials that Alpharma had created.[95] Then, on February 18, 2010, Allergan received a warning letter regarding those materials.[96] As discussed in detail below, Allergan took prompt corrective action in response to the warning letter. As part of its response, Allergan hired a consultant named Jennifer Altier to create new marketing materials.[97] Ms. Altier testified that, after the warning letter, Allergan "took a very conservative approach"; specifically, she described the marketing materials as a "colorful [package insert ("PI")]," and she testified that they were "really just reflective of the information that was in the PI, sticking with the label, remaining within the FDA guidelines."[98] Professor Perri confirmed that numerous Kadian marketing materials contained statements taken directly from the FDA approval letter for Kadian and the Kadian PI.[99] Those materials also were submitted to the FDA for its review prior to use.[100]

(52) Professor Perri also admits that Kadian marketing materials show that sales representatives "were specifically directed to discuss safety considerations with prescribers during sales calls."[101] In fact, Professor Perri cites a presentation given at the 2011 National Sales Meeting for Kadian.[102] That presentation contains a "Do's" and "Don'ts" section. Under the "Do's" section, Allergan instructed the sales representatives to "discuss safety considerations associated with Kadian with prescribers during sales calls," and to "communicate the full indication for Kadian during discussions with prescribers."[103] Under the "Don'ts" section, Allergan instructed the sales representatives not to make comparative product claims or unsubstantiated efficacy claims: specifically, Allergan explained that there is no substantial evidence demonstrating that Kadian improves functioning or quality of life, and thus, the sales representatives were prohibited from making that kind of claim.[104] Numerous Kadian training presentations include similar instructions.[105]

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93 Leitch Dep. at 61:5–10.

94 Leitch Dep. at 100:1–19; *See also* Altier Dep. at 369:19–370:1; Leitch Dep. at 44:20–45:11; "Given patents for the product expire in April 2010, our strategy needed to be a greatly rationalized approach versus what Alpharma had done in the past." *See* ALLERGAN_MDL_01692522 at 2522–2524.

95 Leitch Dep. at 127:10–17.

96 ALLERGAN_MDL_00795835 at -5835-5847; Altier Dep. at 83:5–14.

97 Altier Dep. at 367:2–7.

98 Altier Dep. at 94:22–95:9; *See also* Perri April 24 Dep. at 614:13–24.

99 Perri Dep. at 581:10–596:4 (objections omitted).

100 Boothe Dep. at 170:17–171:7.

101 Perri Rep. ¶ 123.

102 Perri Rep. fn 246.

103 ACTAVIS0413281 at -3293.

104 ACTAVIS0413281 at -3296.

105 *See e.g.*, ALLERGAN_MDL_00405530 at -5566–5572; ALLERGAN_MDL_01199237 at -9247–9250;

(53) In September 2010, Allergan expanded the salesforce from 18 representatives to 46 representatives, and 2 managers to 4 managers.[106] The reason for the expansion was that Kadian's remaining product life had increased given that no generic competitors had released a generic version of Kadian at the time of patent expiration.[107] The goal of increasing awareness about Kadian remained.[108]

(54) At the end of 2012, Actavis merged with Watson Pharmaceuticals. After the merger, Watson made the decision to release the salesforce.[109] Allergan's relationship with Ventiv thus terminated at the end of the year on December 31, 2012.[110] No in-person detailing was conducted after this date.

(55) Allergan also engaged two telemarketing firms to promote Kadian. The first one was called TMS Health, which Allergan hired on April 23, 2009.[111] Allergan provided the TMS sales representatives with a telemarketing script that they were required to follow.[112] Allergan terminated its agreement with TMS effective September 15, 2012.[113]

(56) Allergan also engaged Technekes on June 6, 2012.[114] Technekes originally was retained for purposes of promoting MoxDuo,[115] but because MoxDuo was never approved, Allergan contracted with Technekes to promote Kadian, particularly by filling prescribers' requests for co-pay cards.[116] Allergan's contract with Technekes lasted until December 31, 2013, and was not renewed.[117]

(57) Although in-person detailing and telemarketing calls constituted the bulk of Allergan's promotional activities for Kadian, Allegan engaged in limited other marketing efforts. For instance, Allergan hired a company called Triple i to send Kadian copay materials to prescribers and pharmacies and to communicate Allergan's acquisition of Kadian to these recipients.[118] Allergan also engaged a company called Adheris to institute an adherence program, which consisted of sending letters to

ALLERGAN_MDL_00418211 at -8222–8223.

106 Leitch Dep. at 66:2–7, 68:8–11, 179:17–180:1; ALLERGAN_MDL_01736991 at -6992.

107 ALLERGAN_MDL_01736991 at -6992.

108 ALLERGAN_MDL_01736991 at -6992.

109 Altier Dep. at 370:2–8.

110 *See* Allergan's Fourth Amended Objections and Responses to Plaintiffs' Corrected Second Set of Interrogatories, *In re National Prescription Opiate Litigation*, MDL No. 2804, Case No. 17-md-2804 (N.D.Ohio Mar. 4, 2019.) pp. 35–38.

111 ALLERGAN_MDL_01782063 at -2063-2088.

112 ALLERGAN_MDL_01782063 at -2067.

113 ALLERGAN_MDL_01746316 at -6316.

114 ALLERGAN_MDL_01447720 at 7720-7729.

115 *See* ALLERGAN_MDL_01447731 at 7731.

116 ALLERGAN_MDL_00076479 at -6479-6485; ALLERGAN_MDL_00385948 at -5948-5952; ALLERGAN_MDL_01862247 at -2247-2252.

117 ALLERGAN_MDL_01862247 at -2249.

118 ALLERGAN_MDL_01891508 at -1508-1531.

Kadian patients providing tips for managing pain, timely refill reminders, and information about how to take Kadian properly.[119]

(58) As I explain in Section III.B, because of Allergan's sole focus on detailing to the exclusion of other forms of alleged unlawful conduct, Professor Rosenthal's model is not "conservative" with regard to Allergan because her model focuses solely on detailing visits, and it therefore overestimates the volume of MMEs attributed to allegedly unlawful marketing by Allergan.

II.C.2. Allergan testimony and documents demonstrate Kadian promotional objectives were focused on maintaining market share and substitution, not market expansion

(59) Professor Perri asserts that the manufacturer defendants attempted to expand the opioid market.[120] He explains that "[a] market expansion strategy is one that offers a product (or service) to existing customers in new ways, or to new customers with the goal of increased sales. Regarding opioid medications, this could mean selling more opioids to existing patients or finding new patients to treat with opioids."[121] However, Professor Perri also acknowledges that promotion may result in "rivalrous" marketing or business substitution, not market expansion. He states, "From a marketing perspective, market expansion and capturing share (market penetration) are not mutually exclusive goals."[122] My review of Allergan's documents and deposition transcripts shows that its promotion objectives focused on maintaining its existing prescriptions and substituting business from existing products, such as Kadian's extended-release morphine competitors, not expanding opioid prescribing by encouraging prescribers to write more opioids overall.

(60) For example, in response to a question about how target lists were developed, Jennifer Altier explained that, generally, "you would look at who was already prescribing the product. And since the strategy was to maintain the share, you would call on those same prescribers."[123] Julie Snyder (Allergan's Rule 30(b)(6) witness) likewise testified that "the overall goal for when Actavis…acquired Kadian was to maintain the sales, maintain the prescription levels. So, really, what they were looking to do was to identify…those physicians that were…the top Kadian prescribers. And those were the ones that the representatives would call on."[124] In addition, Nathalie Leitch explained that Allergan's "main goal was just to make prescribers aware…that Kadian was

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[119] ALLERGAN_MDL_00450170; Acquired_Actavis_00180396; Acquired_Actavis_00180399; Acquired_Actavis_00180401; Acquired_Actavis_00180403; Leitch Dep. at 54:8–17 (objection omitted).

[120] Deposition of Matthew Perri, III, BS Pharm, Ph.D., Rph, April 23, 2019 [hereinafter "Perri Dep. 1/2"] at 172:20–173:3; Perri Rep. ¶ 43.

[121] Perri Rep. fn 51. (emphasis added).

[122] Perri Rep. ¶ 43.

[123] Altier Dep. at 65:22–66:15 (objections omitted).

[124] Deposition of Julie Snyder, November 2, 2018 [hereinafter "Snyder Dep."] at 334:14–336:21.

available," and thus, "it made sense…to talk to…prescribers who had written prescriptions for the product before."[125] In 2009, when Allergan hired Ventiv to detail Kadian, Allergan made clear that its strategy for stemming the decline in Kadian prescriptions was to target Kadian prescribers.[126] That strategy continued into 2011, when Allergan told its sales representatives that, "[t]o meet and exceed our quota, we must continue to get Kadian scripts from our loyalists."[127]

(61) The evidence I have seen also indicates that Allergan targeted prescribers with the objective of taking business from other products, such as MS Contin and other versions of morphine. In response to the question whether Allergan targeted high-volume prescribers, Doug Boothe explained, "As part of our sales targeting, which again is common for all pharmaceutical companies, you look at who are prescribing, and not just Kadian, but who are prescribing drugs in that class. This is the pain class. And that's essentially where you would target your sales representatives to call on a more frequent basis."[128]

(62) Allergan's promotional materials and training presentations further confirm Allergan's strategy to target existing opioid prescribers. Allergan received an FDA warning letter in part because Allergan's sales representatives were using a promotional piece called a "Comparison Detailer."[129] This marketing piece states, "Why settle for generic MS Contin tablets…[w]hen you can prescribe the benefits of KADIAN capsules?"[130] In addition, it compares the blood plasma levels, pain control, and sleep scores when patients take Kadian as opposed to generic morphine.[131] This material was focused on patients switching from one long-acting morphine product to another, not on patients who otherwise would not be taking an opioid.

(63) After Allergan received the warning letter, its sales representatives ceased using the Comparison Detailer and were specifically instructed not to make comparative product claims.[132] Even so, Allergan continued to focus on switching opioid prescribers to Kadian without making comparative claims. For instance, Allergan used a training module called the "Objection Handling Workshop," which trained the sales representatives on how to manage pushback from prescribers on various topics.[133] One type of objection that Allergan thought its sales representatives might hear is "[w]hy should I switch my patients to Kadian? They are doing fine on other long acting opioids."[134] To that,

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125 Leitch Dep. at 44:20–45:14.

126 ALLERGAN_MDL_01112578 at -2578; ALLERGAN_MDL_01112579 at -2580.

127 ALLERGAN_MDL_00402219 at 4; *See also* ALLERGAN_MDL_00397937 at 4 (explaining that the initial goal "was to stabilize Kadian sales by calling on the highest volume Kadian writers").

128 Boothe Dep. at 164:18–165:9 (objections omitted).

129 ALLERGAN_MDL_01103851 at 3851–3852.

130 ALLERGAN_MDL_01103851 at 3851–3852.

131 ALLERGAN_MDL_01103851 at 3851–3852.

132 *See, e.g.*, ACTAVIS0413281 at -3296.

133 ALLERGAN_MDL_00405512.

134 ALLERGAN_MDL_00405512 at 17.

the sales representatives were instructed to respond that they were permitted to provide information about Kadian, not to discuss other long-acting opioids[135] As Professor Perri admits, many (if not all) of the statements in the Objection Handling Workshop come directly from the FDA approval letter for Kadian or the Kadian package insert (PI).[136]

(64) Allergan recognized that its "targeting focus can't be so narrow that we miss opportunities with targets who write a little Kadian BUT large amounts of morphine (i.e. morphine sulfate, Avinza)."[137] Thus, Allergan decided to target high morphine and Avinza writers in addition to high generic morphine writers.[138] In fact, Allergan hired additional representatives called "Area Business Specialists" who were specifically "charged with targeting high volume prescribers of generic morphine sulfate who are currently prescribing little to no Kadian and turning them into Kadian prescribers. This expansion is an extension of our overall strategy to capture prescriptions that might otherwise go to the generic product."[139]

(65) In sum, I am not aware of evidence that Allergan's promotional focus was to start patients on Kadian who would not otherwise be prescribed an opioid.

II.C.3. Kadian corrective action

(66) On February 18, 2010, the FDA issued a warning letter to Allergan claiming that two Kadian promotional materials—a "Co-Pay Assistance Program brochure"[140] and a "PK to PK Comparison Detailer"[141]—contained false or misleading information for allegedly (1) omitting and minimizing risk information, (2) broadening the Kadian indication and failing to state the full Kadian indication, (3) making unsubstantiated superiority claims, and (4) containing unsubstantiated effectiveness claims.[142] Allergan took corrective action almost immediately after receiving the warning letter. Below I provide a timeline of events concerning Allergan's response:

- **February 19**: Allergan forwarded the warning letter to the sales representatives instructing them to "immediately cease" disseminating these materials and to quarantine all Kadian promotional materials in the field until further notice because they too could contain messages similar to those

[135] *See* ALLERGAN_MDL_00405512.

[136] Perri Dep. at 581:10–596:4 (objections omitted).

[137] ALLERGAN_MDL_00402219 at 7.

[138] ALLERGAN_MDL_00402219 at 13; *See also* ALLERGAN_MDL_00397937 at 16 (noting that Actavis's goal was to maximize Kadian sales "by converting high volume MS prescribers to Kadian."); ACTAVIS0197924 at 34–35 (listing questions that the sales representatives to ask prescribers for purposes of obtaining switches from generic morphine and Avinza without making comparative product claims).

[139] ALLERGAN_MDL_00418998 at -8998.

[140] ALLERGAN_MDL_00440829.

[141] ALLERGAN_MDL_01103851 at 3851–3852.

[142] ALLERGAN_MDL_00795835 at -5835-5847.

at issue in the warning letter. Promotion was permitted to continue, but all promotion had to be limited to the copay cards (without the brochure) and the Kadian PI.[143]

- **February 21**: Ventiv forwarded Allergan's letter and the warning letter to the salesforce, instructing that the team may not use the Kadian promotional materials and explaining that all promotional materials—except the copay card itself and the Kadian PI—had to be held.[144]
- **March 4**: Allergan responded to the FDA warning letter, informing the FDA that the sales representatives were instructed to cease using materials containing the challenged statements and to return them to Allergan for destruction. Allergan also proposed a corrective-action plan, which included proposed "Dear Healthcare Professional" and "Dear Consumer" letters to be sent to those who had received the offending promotional materials.[145]
- **March 9**: Allergan instructed the Kadian sales representatives to return all promotional materials either in their possession or that could be obtained for destruction.[146]
- **March 26**: FDA responded to Allergan's March 4 letter, generally agreeing with Allergan's corrective-action plan and requesting that Allergan send the proposed "Dear Healthcare Letter" to anyone who could have received the Comparison Detailer.[147]
- **April 9**: Allergan responded to the FDA's March 26 letter confirming that the "Dear Healthcare Letter" would be sent to any prescriber that could have been exposed to the Comparison Detailer. Allergan also recommended sending the "Dear Consumer" letters to patients directly or to physicians' offices.[148]
- **April 19**: FDA responded to Allergan's April 9 letter, requesting that Allergan deliver 100 copies of the "Dear Consumer" letter to prescribers and that physicians have these letters for 90 days.[149]
- **May 3**: Allergan responded to the FDA's April 19 letter, agreeing to the FDA's plan. Allergan also promised to call any prescribers not personally visited to see if the prescribers needed additional letters.[150]

[143] ALLERGAN_MDL_01869494; ALLERGAN_MDL_01869495; ALLERGAN_MDL_01869507.
[144] ALLERGAN_MDL_01869510 at 9510–9511;
ALLERGAN_MDL_01869512;
ALLERGAN_MDL_01869524.
[145] ALLERGAN_MDL_01396751.
[146] ALLERGAN_MDL_01436179.
[147] ALLERGAN_MDL_01866384.
[148] ALLERGAN_MDL_01399387.
[149] ALLERGAN_MDL_01874806.
[150] ALLERGAN_MDL_01875958.

- **May 20**: FDA responded to Allergan's May 3 letter, requesting that Allergan "physically visit" each prescriber to set up a stand with the "Dear Consumer" letters, and to follow up with the prescribers by calling them each month for 90 days.[151]
- **June 10**: Allergan responded to the FDA's May 20 letter, again agreeing to the FDA's proposed plan and committing to personally visit roughly 10,000 prescriber offices and over 550 pharmacies that had received copay materials from Allergan. Allergan would temporarily expand its sales team to accomplish this corrective action.[152]
- **June 29**: Allergan sent TMS Health a revised telemarketing script to account for the warning letter's concerns.[153]
- **July 6**: FDA responded to Allergan's June 10 letter, agreeing with Allergan's plan regarding the "Dear Doctor" letter. FDA also agreed with Allergan's intentions of mailing the "Dear Healthcare Professional" letter to those prescribers who might have received the Comparison Detailer.[154]
- **July 7–8**: Allergan trained new sales representatives with the corrected message.[155] Training included presentations on the Kadian PI,[156] Kadian marketing materials,[157] objection handling,[158] and Kadian support programs.[159]
- **July 16**: Allergan responded to the FDA's July 6 letter explaining that 7,163 physicians would be receiving "Dear Healthcare Professional" letters via mail.[160]
- **August 4**: FDA responded to Allergan's July 16 letter, signing off on Allergan's plan.[161] In addition, Allergan conducted corrective-message training for its sales representatives.[162]
- **August 10**: Allergan informed Ventiv that, during the corrective-action period, the sales representatives were prohibited from making regular sales calls. Allergan further explained that it will be mailing a "Dear Healthcare Professional" letter to all healthcare professionals who potentially received the Comparison Detailer, and that the sales representatives would hand deliver copies of the "Dear Consumer" letter to prescribers and pharmacies that received the Co-

151 ALLERGAN_MDL_01868671.
152 ALLERGAN_MDL_01399410 at -9411.
153 ALLERGAN_MDL_00436590.
154 ALLERGAN_MDL_01869099.
155 ALLERGAN_MDL_01897644.
156 ALLERGAN_MDL_00405530 at -5530-5572.
157 ALLERGAN_MDL_00435872.
158 ALLERGAN_MDL_00405512.
159 ALLERGAN_MDL_00405573.
160 ALLERGAN_MDL_01237743 at -7743–7762.
161 ALLERGAN_MDL_01238281 at -8281–8284.
162 ALLERGAN_MDL_01051295 at 1295–1333.

Pay Assistance Program brochure. To accomplish this corrective action, Allergan would hire an additional 175 temporary sales representatives.[163]

- **August 18**: Allergan finalizes the "Dear Healthcare Professional"[164] and "Dear Consumer"[165] letters for submission to the FDA.
- **August 19**: Allergan and Ventiv conducted corrective-action rollout training for the salesforce.[166]
- **August 23**: The corrective-action campaign began. Sales representatives were prohibited from making regular sales calls during this time.[167]
- **September 10**: Although the sales representatives had nearly completed their corrective-action campaign, they were instructed not to resume promotion until Allergan gave permission.[168]
- **September 26:** Allergan informed the sales representatives that Kadian promotional activities were permitted to resume "only if you have completed dissemination of the corrective action materials to all of your targets."[169]
- **November 1**: Allergan informed the FDA that it had completed disseminating the "Dear Healthcare Professional" and "Dear Consumer" letters and that the salesforce would be conducting follow-up calls to each prescriber and pharmacy.[170]

[163] ALLERGAN_MDL_01110478 at 0478–0480.
[164] ALLERGAN_MDL_01110407 at 0407–0413.
[165] ALLERGAN_MDL_01110403 at 0403–0406.
[166] ALLERGAN_MDL_00435497 at -5497–5526.
[167] ALLERGAN_MDL_01115903 at -5903–5910.
[168] ALLERGAN_MDL_01897894 at -7894.
[169] ALLERGAN_MDL_01419292 at -9292. (emphasis in original).
[170] ALLERGAN_MDL_02106570 at -6570.

III. Professor Rosenthal ignores the limited scope and nature of Allergan's promotion

(67) Plaintiffs' economic experts rely on flawed causation and damage methodologies that purport to calculate the harm resulting from the "combined effect of the Defendant manufacturers' promotion" by assuming that (1) all defendant promotion since 1995 is unlawful (based upon counsel instruction) and (2) all defendant promotion had the same effects on prescribing (based upon the construction of Professor Rosenthal's model).[171] Professor Rosenthal concedes that her model does not separately assess the extent to which Allergan's or any manufacturer's conduct specifically expanded opioid MMEs.

> Q. What if a manufacturer engages only in limited detailing and not other types of promotional activities? It would not be conservative for that manufacturer to only look at detailing, correct?
>
> A. The purpose of my analysis is not to assign liability to individual defendants. It's to look at the aggregate effect. So I don't know what would be appropriate. That to me seems like a legal question.
>
> Q. Would it be conservative from an economic perspective if a manufacturer purchases an opioid product in, say, 2008 and engages in detailing but no other marketing?
>
> A. I do not calculate any estimates at the individual defendant level, so I cannot characterize them as conservative or otherwise. I'm only looking at aggregate effects.[172]

By combining Allergan with all other defendants in their models and assigning the average aggregate effect to Allergan's limited promotional efforts, Plaintiffs' economic experts ignore the following factors that differentiate Allergan:

- Allergan's Kadian and Norco detailing constituted a small share of all opioid-related detailing, and the depreciated stock of Allergan detailing as captured by Professor Rosenthal contributes almost nothing to Professor Rosenthal's overall depreciated detailing stock.
- The types of promotion Allergan employed were much more limited than the types described by Professor Rosenthal and other Plaintiff experts.

[171] Professor Rosenthal's model makes this assumption despite numerous studies cited in IV.C. of her report that demonstrate otherwise. *See, e.g.*, Rosenthal Report ¶ 33 ("Berndt, et al. distinguish between 'industry expanding' and 'rivalrous' marketing efforts").

[172] Rosenthal May 4 Dep. at 193:20–194:14.

- Nearly all of the documents Plaintiffs or their experts identify with respect to Allergan promotion relate to Kadian. However, Allergan's Kadian detailing from 2009–2013 was far more limited than Alpharma's marketing during the prior time period, and 85% of it occurred after Allergan began disseminating FDA-approved labeling and corrective messaging.

Given these Allergan-specific distinctions, Plaintiffs' economic experts have no basis on which to opine that Allergan's promotion was unlawful, and their models are incapable of distinguishing between the effects of Allergan's relatively limited promotion and any other promotion, lawful or not. Moreover, Kadian and Norco account for an extremely small share of opioid MMEs in Cuyahoga and Summit counties, and nationally, which underscore the limited scope and magnitude of Allergan's promotion of these two products.

III.A. Allergan's detailing constituted a small share of all opioid-related detailing, and it is not material to Professor Rosenthal's results

(68) In Figure 3, I illustrate Allergan's detailing for Norco and Kadian in the context of detailing conducted by all other defendants and by non-defendants.[173] Allergan's detailing of Norco began in 1997, approximately 20 years after "the pharmaceutical industry began to market codeine, hydrocodone, and oxycodone products in combination with aspirin or acetaminophen, under trade names such as Tylenol with Codeine (including multiple strengths of the codeine component) Vicodin and Percocet."[174] Like Norco, Vicodin is a combination of hydrocodone and acetaminophen. Similarly, Percocet is a combination of hydrocodone and ibuprofen. According to Professor Perri, a number of other notable events occurred prior to Norco's detailing, including:

- In about 1987, "Purdue's MS Contin (extended release morphine sulfate), which at the time did not have approval from the FDA as a new drug, was marketed as a 'generic' morphine product prior to its formal approval under a new drug application by the FDA."[175]
- "In 1991, a unique product, Duragesic (fentanyl transdermal patch), was introduced to provide long-acting delivery of fentanyl for patients who needed sustained analgesia."[176]
- "By 1995, Purdue had developed extensive marketing plans for the launch of OxyContin. This planning was effective as Purdue's OxyContin sales increased to nearly $1 billion in 2000 and

[173] I rely on Professor Rosenthal's defendant and non-defendant designations, except that for purposes of Figure 3, I include Combunox, Lorcet, Maxidone, and Reprexain in the Non-Defendant segment of the bars for the reasons discussed above. I also analyze these drugs along with Kadian and Norco, as seen in my backup data, and I reach the same conclusions as those reflected in this report.

[174] Perri Rep. ¶ 103.

[175] Perri Rep. ¶ 104.

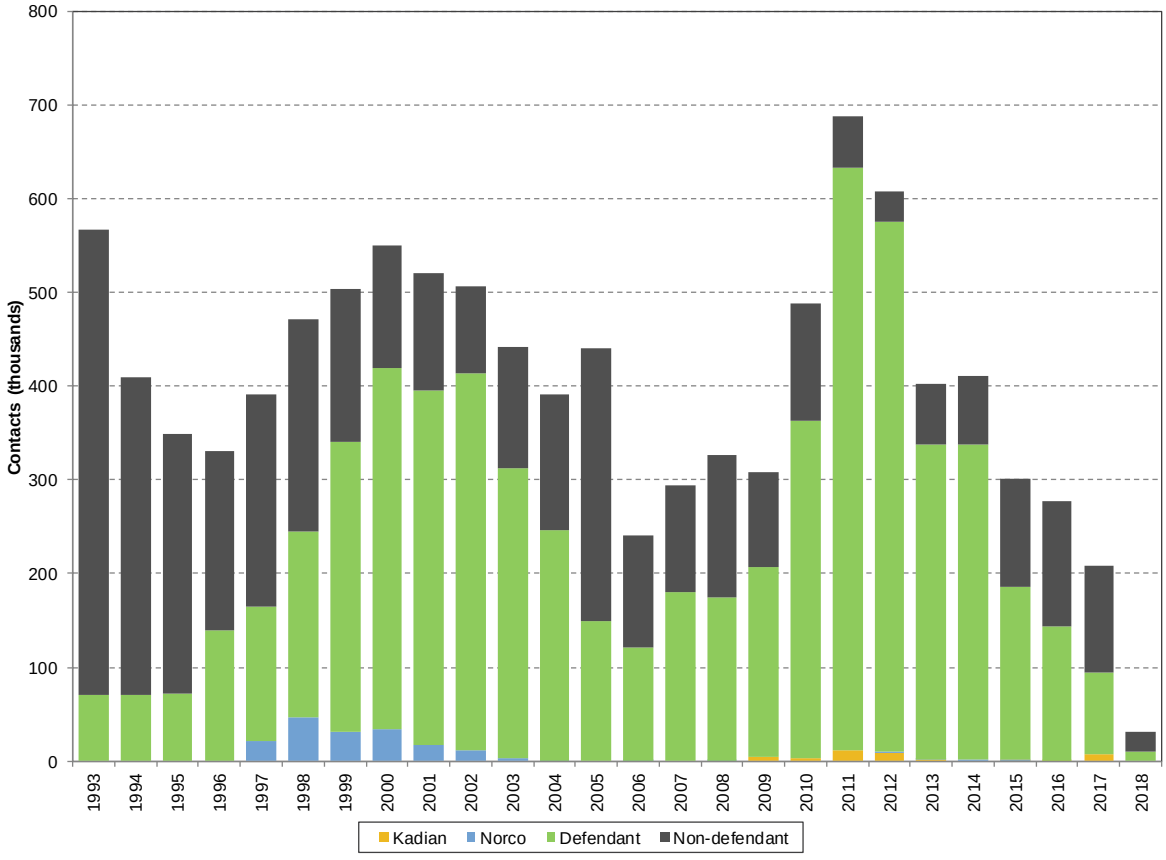
[176] Perri Rep. ¶ 105.

estimated sales in excess of $1.3 billion in 2001. During about the same time period, Purdue's sales force grew from 256 PSRs in 1995 to 674 PSRs in 2000."[177]

Allergan's detailing efforts for Norco increased in 1998, but still accounted for less than 10% of all opioid detailing. Thereafter, Norco detailing declined in terms of the count of contacts and the percentage of all opioid detailing. Norco detailing all but concluded by mid-2003.

(69) Allergan detailed Kadian upon acquiring the product in January 2009, but its detailing was very small compared to other defendant and non-defendant promotion. Kadian detailing accounted for 1%–2% of all opioid detailing from 2009–2012, before it effectively concluded in 2013.

Figure 3: Allergan detailing contacts for Norco and Kadian compared to other defendant and non-defendant detail contacts



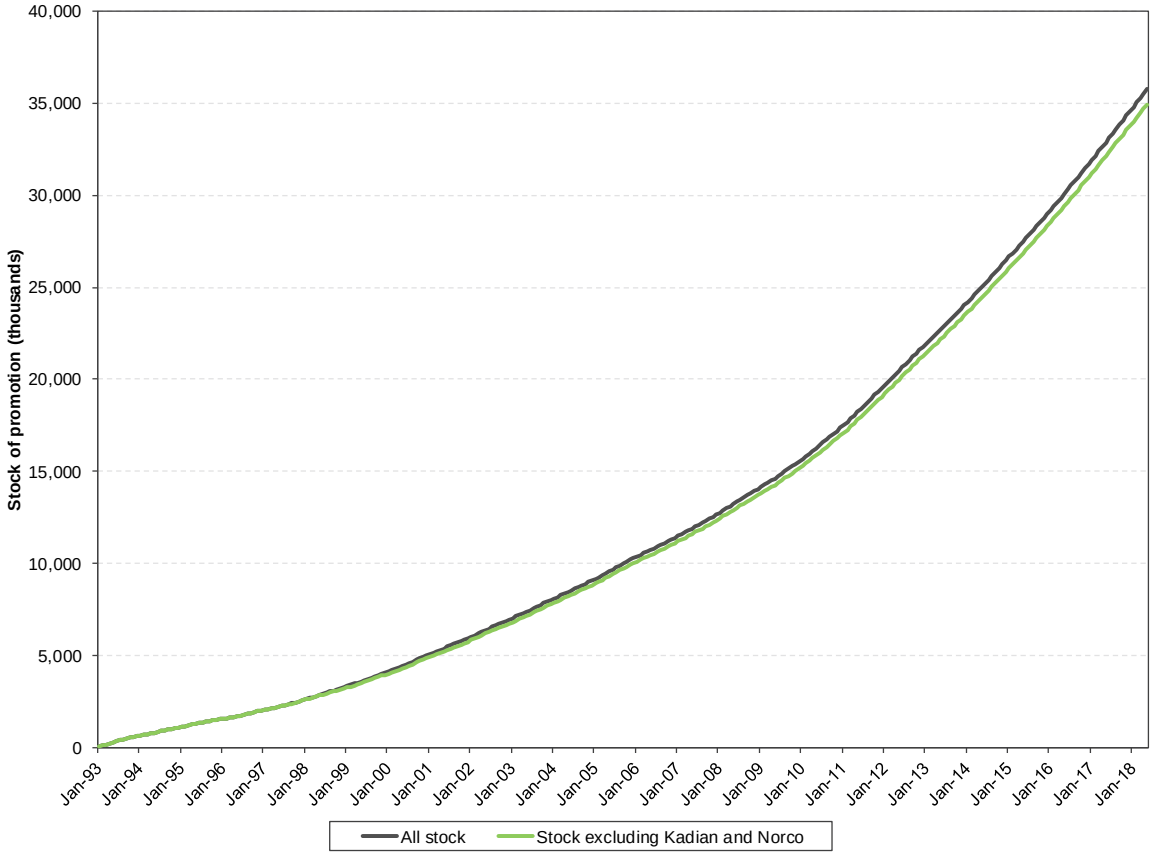
Source: Rosenthal contacts data.

(70) In Figure 4, I illustrate Allergan's detailing in the context of the depreciated marketing stock Professor Rosenthal calculates using all opioid detailing. The top, black line in Figure 4 reflects the stock of all defendant detailing contacts included in Professor Rosenthal's direct model, depreciated

[177] Perri Rep. ¶ 107; PPLPC012000371063 at slide 2.

monthly by the -0.0067 rate yielded by her model. The lower, green line reflects the depreciated detailing stock of all defendants after excluding Allergan's detailing. As shown, the depreciated detailing stock without Allergan is just slightly below and almost perfectly correlated with the total.[178] This demonstrates that Professor Rosenthal would reach essentially the same result in the absence of Allergan's detailing, and that Plaintiffs' experts cannot reliably conclude that Allergan's detailing caused any of the harms that they attribute to manufacturer conduct.

Figure 4: Professor Rosenthal's depreciated detailing stock with and without Norco and Kadian



Source: Rosenthal backup data.

[178] The correlation coefficient between the depreciated detailing stock for all defendants with and without Allergan is 0.999996.

III.B. The types of promotion Allergan employed were much more limited than the types described by Professor Rosenthal and other Plaintiff experts

(71) Professor Rosenthal conducts her models using manufacturer detailing rather than the broad scope of marketing activities that Plaintiffs and their experts allege were conducted by the manufacturer defendants. She explains:

> The manufacturer Defendants used a panoply of both branded and unbranded marketing tactics to increase opioid sales. While documents produced in discovery show many examples of such promotional efforts beyond detailing that I understand Plaintiffs intend to prove were illegal, for the purposes of my econometric analysis, I rely on detailing contacts (i.e., the number of visits to physicians and other providers) to measure promotion for several reasons.[179]

One of the reasons offered by Professor Rosenthal assumes that detailing is a reliable proxy of all types of promotional activity:

> Second, pharmaceutical marketing programs typically combine various forms of marketing such that, were there to be an increase or decrease in promotional detailing, it is reasonable to expect that some other forms followed that course. From an econometric standpoint, detailing is a good proxy for total promotional effort.[180]

(72) However, a model based only on detailing would over-represent manufacturers that perform only detailing and under-represent manufacturers that perform a variety of promotional activities in addition to detailing. The potential bias is even larger if detailing and other types of promotional activities are complementary or synergistic, i.e., if a firm's detailing is even more effective when combined with the recommendation of a KOL or sponsorship of CME events. This renders Professor Rosenthal's model particularly inappropriate with respect to Allergan, which performed few promotional activities beyond detailing.

(73) In Section II.C.1, I explain that Allergan's promotional efforts did not include many of the types identified by Plaintiffs and their experts. For example, I am not aware of any evidence that Allergan distributed free samples; sponsored CME events; influenced treatment algorithms; or participated in unbranded marketing campaigns, advisory boards, or health advocacy groups. Thus, not only does Professor Rosenthal's model fail to distinguish among the effects of marketing conducted by different manufacturers or for different products, its reliance on detailing as a proxy for all promotion

[179] Rosenthal Rep. ¶ 56.

[180] Rosenthal Rep. ¶ 56.

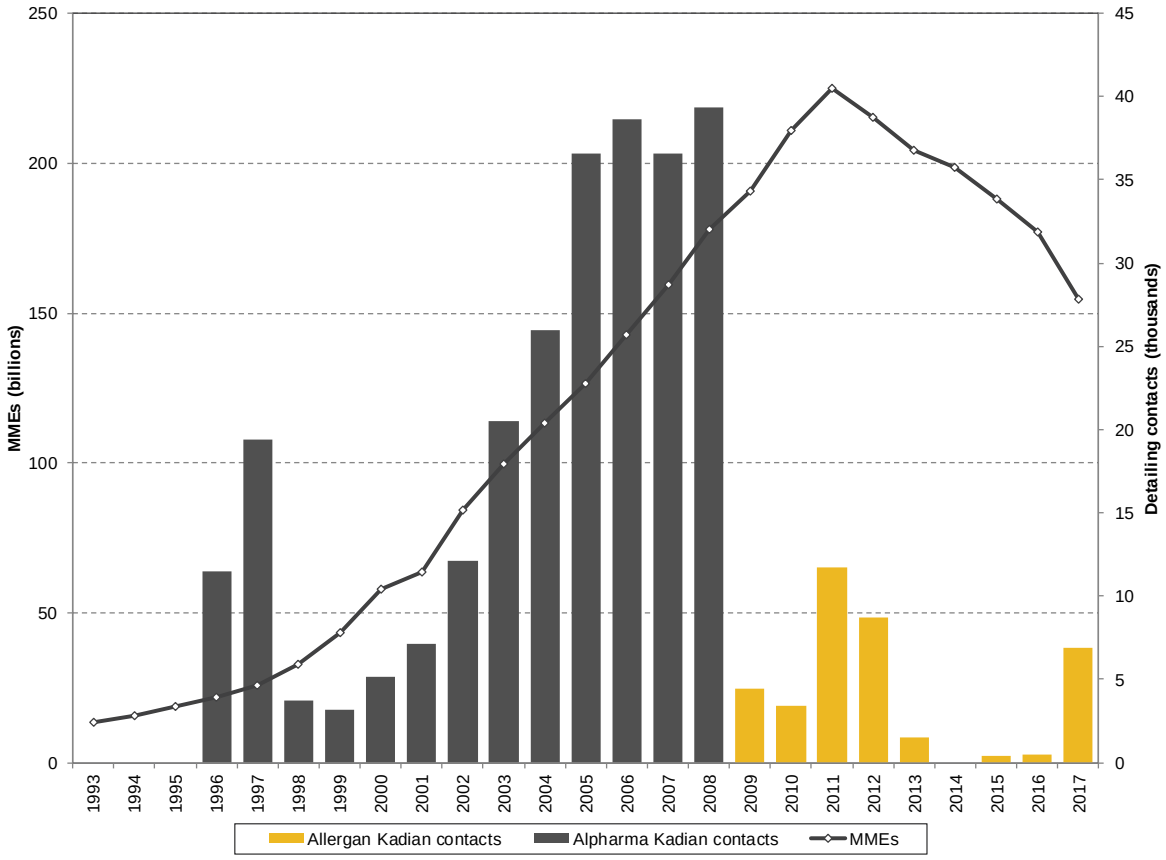
inappropriately attributes more weight to Allergan and other manufacturers who engage in few promotional activities beyond detailing.

III.C. Allergan's Kadian detailing was far more limited than Alpharma's, and most of it occurred with agreement from the FDA

(74) As I explain above in Section II.C, the promotional activities identified by Plaintiffs and their experts with respect to Allergan focus almost entirely on Allergan's promotion of Kadian. I therefore evaluate in this section the nature of Allergan's Kadian detailing. I find that the magnitude of Allergan's Kadian detailing is very small relative to all opioid detailing and to Alpharma's Kadian detailing, and I explain that 85% of Allergan's Kadian detailing occurred during or after corrective action agreed to by the FDA. In conducting her analysis of manufacturer causation, Professor Rosenthal fails to account for the likelihood that the Kadian detailing conducted by Allergan during and after corrective action—pursuant to FDA agreement—is lawful or at the very least less susceptible to wrongdoing compared to the detailing conducted by other defendant and non-defendant manufacturers.

(75) Allergan acquired Kadian in December 2008 and detailed the product in 2009 and 2010, a period when the total number of all opioid MMEs was expanding. During these two years, however, Allergan's Kadian detailing accounted for only 1% of all opioid detailing. As shown in Figure 5, Allergan's Kadian detailing was also just a fraction of the Kadian detailing that had been performed by Alpharma prior to 2009. Specifically, the total number of Allergan Kadian detailing contacts in the four-year period after Allergan's acquisition (2009–2012) was less than 20% of the Alpharma Kadian detailing contacts in the preceding four year-period (2005–2008).

Figure 5: Alpharma and Allergan Kadian detailing compared to total opioid MMEs



Source: Rosenthal backup data. The Kadian call note data produced by Allergan (ALLERGAN_MDL_01890663.xlsx) do not reflect any detailing contacts after 2012, in contrast to the detailing contacts reported after 2012, and in particular in 2017, in the IQVIA IPS data relied upon by Professor Rosenthal. I am not aware of any evidence that suggests that Allergan marketed Kadian in 2017.

(76) Allergan's Kadian detailing more than doubled in 2011 and 2012 relative to its very low levels in 2009 and 2010, as the total number of opioid MMEs began to decline and after Allergan took extensive efforts to respond to a warning letter from the FDA. Indeed, more than 85% of Allergan's Kadian detailing occurred after February 2010, when the Kadian sales force began taking corrective action in response to an FDA warning letter and as agreed upon by the FDA. Plaintiffs' experts assume inappropriately that the detailing Kadian conducted pursuant to the corrective action was both unlawful and had the same effect on opioid MMEs and ultimately on harms suffered by the counties as all other detailing, both by defendant and non-defendant manufacturers, despite the fact that the information relayed during these visits was explicitly agreed to by the FDA. Professor Rosenthal confirms that she included corrective detailing in her model and assumed it was unlawful:

> Q. Let me just ask a simpler question: Yes or no, are details that are simply designed to provide corrective messaging included in your stock of promotion?

A. I really have no idea about whether such details exist. My model includes all detailing over the period from 1995 to 2018 based on the instruction that I was given to consider that unlawful.

Q. Okay. Without distinguishing between the quality or extent of those detailing visits?

A. I do not distinguish among those details, no.[181]

III.D. Allergan's prescription opioids accounted for a fraction of 1% of all prescribed opioids

(77) Kadian and Norco account for an extremely small share of opioid MMEs in Cuyahoga and Summit counties, and nationally. These small shares underscore the limited scope and magnitude of Allergan's promotion of these two products. In Figure 6–Figure 8, I list by year the share of opioid MMEs associated with Kadian and Norco in Cuyahoga and Summit counties, and nationally, respectively. I exclude shares prior to 2009 for Kadian because Alpharma owned and promoted Kadian during that time. Allergan's combined share of opioid MMEs over the time period from January 1997–April 2018 was approximately 0.27% in both Cuyahoga and Summit counties. This is slightly lower than in the rest of the nation, where Allergan's combined share was 0.40%. In Cuyahoga and Summit counties, neither Kadian nor Norco accounted for more than 1% in any year.[182] These figures are consistent with the analysis of Plaintiffs' expert Dr. McCann, who calculates that Allergan shipments account for 0.00% of MMEs in Cuyahoga and Summit counties during the period 2006–2014.[183]

[181] Rosenthal May 4 Dep. at 217:20–218:14 (objections omitted).

[182] I limit my share analysis to 1997–2018 because data with prescriber location are unavailable prior to 1997.

[183] Second Supplemental Report of Craig J. McCann, April 15, 2019 at Appendix 1.

Figure 6: Allergan product shares of all opioid MMEs in Cuyahoga County, by year[184]

Year	Kadian	Norco	Total
1997		0.00%	0.00%
1998		0.19%	0.19%
1999		0.58%	0.58%
2000		0.61%	0.61%
2001		0.19%	0.19%
2002		0.19%	0.19%
2003		0.13%	0.13%
2004		0.09%	0.09%
2005		0.09%	0.09%
2006		0.06%	0.06%
2007		0.04%	0.04%
2008		0.03%	0.03%
2009	0.94%	0.02%	0.96%
2010	0.72%	0.02%	0.74%
2011	0.65%	0.01%	0.66%
2012	0.13%	0.01%	0.15%
2013	0.07%	0.03%	0.10%
2014	0.07%	0.02%	0.08%
2015	0.06%	0.01%	0.08%
2016	0.06%	0.01%	0.08%
2017	0.07%	0.01%	0.08%
1997-2017	**0.20%**	**0.06%**	**0.26%**

Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data.

[184] I include in the denominator of my share calculations in Figures 6–8 the same opioid products that were analyzed by Professor Rosenthal, which I understand includes opioid products that were at any point classified as Schedule II, plus Butrans. Throughout this report, my references to "opioids" are limited accordingly unless otherwise noted. (In her report, Professor Rosenthal incorrectly describes her limitation as including only "class II *oral* opioid products plus Butrans." However, her Appendix C tables and backup production clearly include non-oral opioids, such as Duragesic.) *See* Rosenthal Rep. Table C.5, C.6.

Figure 7: Allergan product shares of all opioid MMEs in Summit County, by year

Year	Kadian	Norco	Total
1997		0.00%	0.00%
1998		0.17%	0.17%
1999		0.30%	0.30%
2000		0.17%	0.17%
2001		0.17%	0.17%
2002		0.18%	0.18%
2003		0.13%	0.13%
2004		0.08%	0.08%
2005		0.08%	0.08%
2006		0.06%	0.06%
2007		0.06%	0.06%
2008		0.04%	0.04%
2009	0.77%	0.02%	0.79%
2010	0.76%	0.02%	0.78%
2011	0.76%	0.01%	0.77%
2012	0.20%	0.02%	0.21%
2013	0.14%	0.03%	0.17%
2014	0.05%	0.03%	0.08%
2015	0.02%	0.02%	0.04%
2016	0.02%	0.01%	0.04%
2017	0.02%	0.01%	0.03%
1997-2017	**0.21%**	**0.06%**	**0.27%**

Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data.

Figure 8: Allergan product shares of all opioid MMEs in the United States

Year	Kadian	Norco	Total
1997		0.20%	0.20%
1998		0.92%	0.92%
1999		1.52%	1.52%
2000		1.29%	1.29%
2001		0.48%	0.48%
2002		0.39%	0.39%
2003		0.23%	0.23%
2004		0.15%	0.15%
2005		0.12%	0.12%
2006		0.11%	0.11%
2007		0.09%	0.09%
2008		0.08%	0.08%
2009	1.06%	0.07%	1.13%
2010	0.86%	0.06%	0.93%
2011	0.76%	0.05%	0.81%
2012	0.28%	0.04%	0.32%
2013	0.18%	0.12%	0.30%
2014	0.10%	0.05%	0.15%
2015	0.06%	0.04%	0.10%
2016	0.07%	0.03%	0.10%
2017	0.05%	0.03%	0.08%
1997-2017	**0.25%**	**0.15%**	**0.40%**

Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data.

(78) To further demonstrate Allergan's limited contribution to overall opioid prescribing, in Figure 9 I superimpose Allergan combined Kadian and Norco MMEs on Professor Rosenthal's graph of her preferred causation model.[185] The dark blue line represents actual monthly MMEs for all opioid prescriptions analyzed by Professor Rosenthal, and the green line represents the number of MMEs that Professor Rosenthal predicts would have been prescribed in the absence of *any* defendant promotion (i.e., the opioid volume that is not attributable to the alleged misconduct). The light blue line that is barely visible at the bottom represents total MMEs for Kadian and Norco combined.

(79) Even immediately following Allergan's acquisition of Kadian, Allergan MMEs total only 3% of the number of MMEs that Professor Rosenthal predicts would have been prescribed in the absence of defendant promotion. Also, because Professor Rosenthal's model is an aggregate one that does not differentiate among manufacturers, she is unable to determine which specific prescriptions in her model are attributed to the alleged misconduct (i.e., whether they fall above or below the green

[185] Rosenthal Rep. Figure D.2.

line).[186] Further, Professor Rosenthal agrees that she has not formed any opinions about whether her purported increase in prescribing was medically unnecessary:

> Q. I understand. Now, you also testified yesterday that you've not formed any opinions about whether any quantity of the increase in MMEs identified in your opinions was medically necessary or unnecessary, correct…On the direct model, do you recall that testimony?
>
> A. Yes. In the direct and indirect models, I do not differentiate between medically necessary and unnecessary prescriptions.[187]

Because of Allergan's small size and the inability of Professor Rosenthal's model to differentiate among manufacturers, Professor Rosenthal cannot opine and Plaintiffs cannot demonstrate that even one of the already *de minimis* Allergan prescriptions were written as a result of (or would not have been written in the absence of) the alleged misconduct.[188]

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[186] In Section IV.A, I discuss further Professor Rosenthal's model's inability to differentiate between manufacturers. *See also* Rosenthal May 4 Dep. at 341:7–341:13.

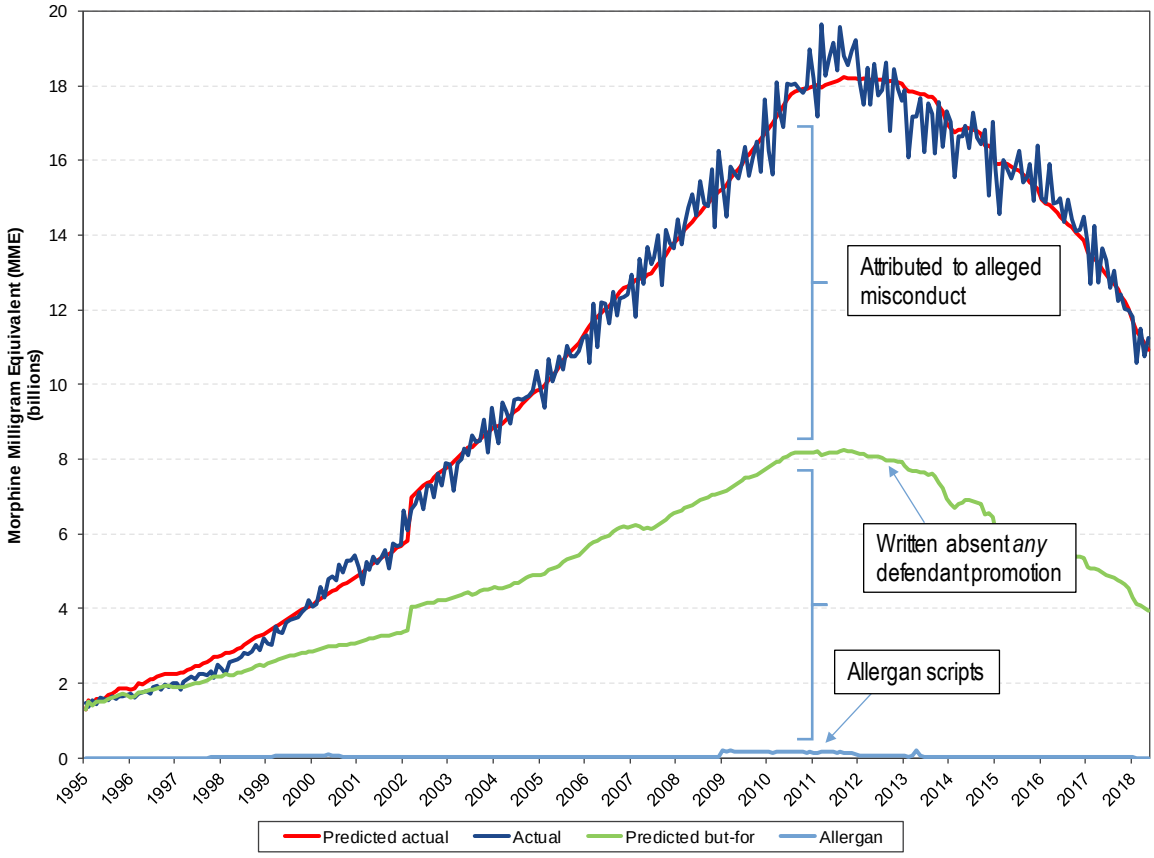
[187] Deposition of Professor Meredith Rosenthal, May 5, 2019 [hereinafter "Rosenthal May 5 Dep."] at 754:15-755:4; Professor Rosenthal also states that her model is "agnostic as to whether the prescriptions caused by the unlawful conduct were diverted or not." See Rosenthal May 4 Dep. at 384:1–384:4.

[188] I understand that Plaintiffs have, in response to Manufacturer Interrogatories 6, 7, and 10, designated certain Kadian and Norco prescriptions as "unauthorized, medically unnecessary, ineffective, or harmful" and "written in reliance on…alleged misrepresentations, omissions, or other alleged wrongdoing." I also understand that Dr. Carol Warfield has evaluated those prescriptions from a medical perspective and determined that there is no evidence that any was inappropriate. But even if a fact finder were to conclude that certain Allergan prescriptions were inappropriate, Plaintiffs' experts' model would be unable to assess whether any of those specific prescriptions were written as a result of Allergan's promotional activity.

Plaintiffs The City of Cleveland, County of Cuyahoga, County of Summit and City of Akron's Supplemental Amended Responses and Objections to the Manufacturer Defendants' First Set of Interrogatories, Submitted Pursuant to Discovery Ruling No. 13, *In re National Prescription Opiate Litigation*, MDL No. 2804, Case No. 17-md-2804 (N.D.Ohio December 31, 2018.), 1.

Plaintiffs The County of Cuyahoga, Ohio and State of Ohio Ex Rel, Prosecuting Attorney of Cuyahoga County, Michael C. O'Malley's Amended Responses to the Manufacturer Defendants' and National Retail Pharmacy Defendants' First Set of Interrogatories, *In re National Prescription Opiate Litigation*, MDL No. 2804, Case No. 17-md-2804 (N.D.Ohio November 2, 2018.), 6.

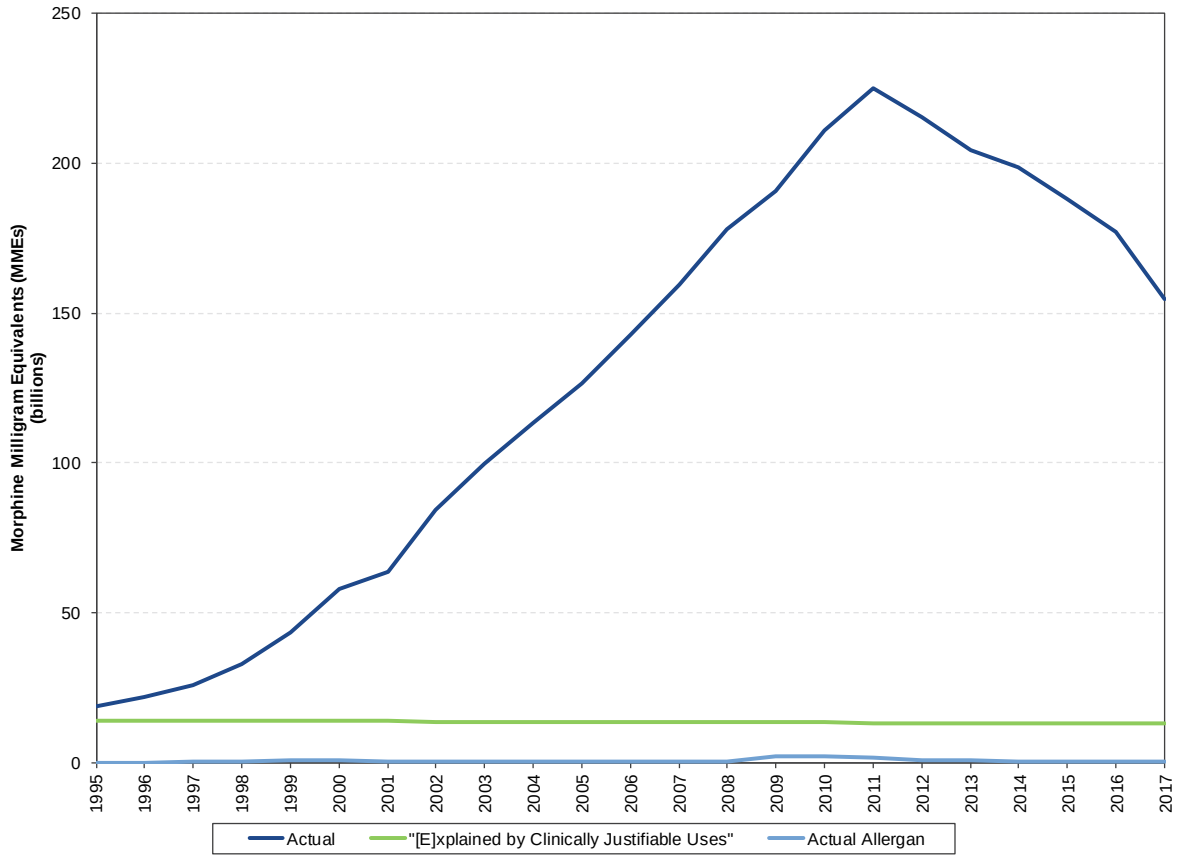
Figure 9: Kadian and Norco MMEs in the context of Professor Rosenthal's preferred direct model



Source: Rosenthal backup data.

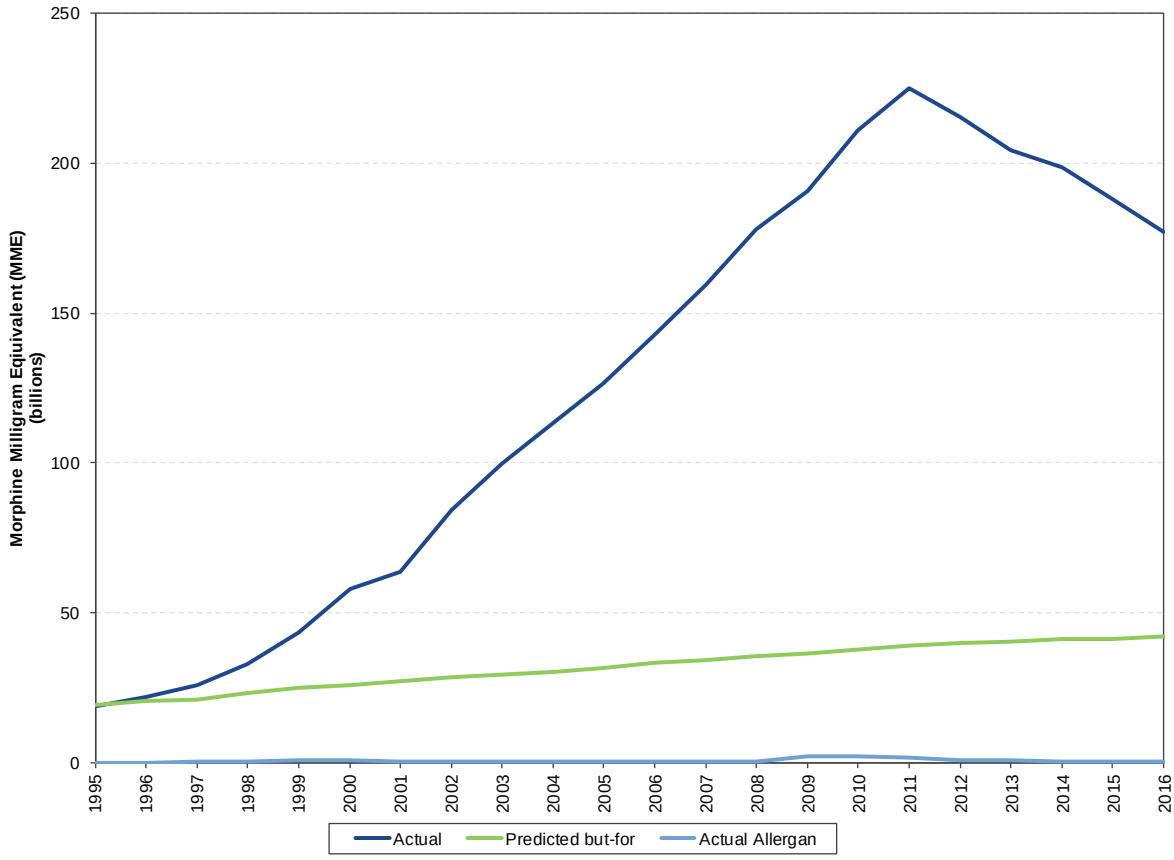
(80) In Figure 10 and Figure 11, I repeat this exercise with Professor Rosenthal's indirect model and "under-treated pain" analysis, respectively. Both of these models also suffer from numerous errors, as I explain in Section VI. But even under Professor Rosenthal's flawed approach, total Allergan MMEs are well below the amount Professor Rosenthal estimates are explained by factors unrelated to the alleged misconduct.

Figure 10: Kadian and Norco MMEs in the context of Professor Rosenthal's indirect model



Source: Rosenthal backup data.

Figure 11: Kadian and Norco MME's in the context of Professor Rosenthal's "maximum…clinically justifiable" analysis



Source: Rosenthal backup data.

(81) Plaintiffs' models cannot credibly conclude that any portion of the alleged harms is attributed to Allergan considering Allergan's extremely small share of all opioid MMEs, particularly in the context of the unquantified uncertainty surrounding the estimates offered by Plaintiffs' economic experts. Although Plaintiffs' economic experts have neglected to quantify this uncertainty, each of their estimates have error bounds that compound when they are multiplied together by Professor McGuire to calculate damages. Even a small level of uncertainty would make it virtually impossible to discern whether Allergan's extremely small share of all opioid MMEs caused any expansion in opioid prescribing.

IV. Plaintiffs have not shown that Allergan's promotion expanded opioid prescribing, let alone improper prescribing

(82) The causation and damages approach offered by Plaintiffs' economic experts purportedly assesses the extent to which increases in manufacturer detailing resulted in *additional* prescribing. Professor Rosenthal explained this in her deposition:

> Q. Does your model account for rivalrous marketing?
>
> …
>
> A. The aggregate model that I put forth is intended to essentially obscure the rivalrous marketing, so to the extent that marketing only moves people from hydrocodone to oxycodone or the other direction, whatever it is, that will show up as a noneffect in my model. So I'm only looking at market expansion because the question I care about is market expansion.[189]

As further discussed below, although Professor Rosenthal claims that rivalrous marketing would show up as a "noneffect" in her model, the reality is that she applies the average effect of detailing to every manufacturer, regardless of whether all of their marketing was rivalrous or none of it was. Because Professor Rosenthal's approach assumes that all detailing has the same incremental effect, it fails to consider whether some detailing (e.g., detailing associated with certain manufacturers, products, or types of products) had no effect on total prescribing or resulted in prescribers switching from opioids they were already prescribing. This has the effect of penalizing defendants whose marketing was primarily rivalrous. In this section, I demonstrate that Plaintiffs' experts have failed to demonstrate that Allergan's promotion expanded opioid prescribing because they have not accounted for the rivalrous nature of that promotion. I also analyze Ohio Automated Reporting Rx Reporting System ("OARRS") data, which Plaintiffs' economic experts have ignored, to demonstrate that prescriber- and patient-specific patterns of Kadian prescribing are consistent with rivalrous marketing and with providers exercising their clinical discretion. I demonstrate the following in this section:

- Professor Rosenthal's models inappropriately assume that all manufacturer promotion equally impacted opioid prescribing.
- Allergan's extremely low share and timing of opioid MMEs in Cuyahoga and Summit counties (i.e., less than 0.3% as listed in Figure 6 and Figure 7) demonstrate that Allergan's promotion did not contribute materially to an overall increase in opioid prescribing.

[189] Rosenthal May 4 Dep. at 206:10–206:25 (objections omitted).

- Allergan deposition testimony and contemporaneous sales documents reflect Allergan's objective to take volume from competing products rather than to expand overall opioid prescribing.
- Provider-specific prescribing and detailing data for Kadian—data ignored by Plaintiffs' economic experts—demonstrate that prescribers Allergan detailed in Cuyahoga or Summit counties routinely did not increase their Kadian prescribing relative to the level of Kadian prescribing prior to Allergan's acquisition from Alpharma.
- Patient-level prescribing patterns for the Allergan-detailed prescribers I was able to identify in the Ohio Automated Reporting Rx Reporting System ("OARRS") data for Cuyahoga and Summit counties reflect that they prescribed Kadian to only a small subset of their patients; that they typically prescribed only a few Kadian scripts per patient, in many instances at low MMEs per day; and that prescribers used discretion when prescribing Kadian, taking patient-specific characteristics into account.

IV.A. Professor Rosenthal assumes that the promotion of all manufacturers, including defendants and non-defendants, equally impacted opioid prescribing

(83) Professor Rosenthal's direct model makes the untested assumption that the promotion of all manufacturers (both defendant and non-defendant) and of all types (using detailing as a proxy), whether lawful or allegedly unlawful, was equally persuasive to physicians to prescribe opioids. This assumption is inconsistent with Plaintiffs' allegations regarding the allegedly deceptive practices of individual defendants described above, and the assumption is not supported by the literature on pharmaceutical promotion. For example:

- Berndt et al. (1995), cited by Professor Rosenthal, note that promotion can be industry expanding or rivalrous, and that the effect of marketing depends on market structure. Specifically, they find that order of entry effects are important, with a strong first-mover advantage. The promotional efforts of later entrants are more likely to be rivalrous, i.e., to substitute for existing products rather than to expand the market. It is therefore not appropriate to assume that all manufacturer promotion affected aggregate shipments in the same way.[190]
- Studies of the economics of advertising, including at least one authored by Professor Rosenthal, often use the theoretical model of Dorfman and Steiner (1954), who derive the optimal advertising to sales ratio as equal to the ratio of the elasticity of sales with respect to advertising and the elasticity of sales with respect to price.[191] In her study, firms vary considerably in the ratio

[190] *See* Ernst R. Berndt, Linda Bui et al., "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," American Economic Review 85, no. 2 (1995), 100–105.

[191] Meredith B. Rosenthal, Ernst R. Berndt, Julie M. Donohue, "Demand Effects of Recent Changes in Prescription Drug Promotion," in Frontiers in Health Policy Research, Vol. 6, eds. David M. Cutler and Alan M. Garber, 1–26

of advertising to sales. This implies that firms are also likely to differ in their elasticity of sales with respect to advertising (i.e., their advertising has differential effects on sales).

- Datta and Dave (2017), also cited by Professor Rosenthal, find that detailing affected brand-specific demand but had no impact on total demand for the class of drugs studied.[192] This study used a much richer dataset than that used by Professor Rosenthal, which allowed the authors to control for other factors that affect prescribing behavior, such as physician characteristics, which Professor Rosenthal ignored.

(84) Professor Rosenthal claims that her model allows for a recalculation of but-for harm if a defendant is exempted from liability because its messages were not found to be unlawful, but key assumptions—namely that all marketing regardless of type, content, or time period has the same impact on sales, and that all incremental sales are equally harmful—are still inherent in her calculations and are never tested. Rather, her sensitivities simply (1) apply the average effects from her aggregate direct model to every manufacturer regardless of the nature of its promotional activity relative to other manufacturers, and (2) scale those effects based on the manufacturer's amount of detailing.[193] This is inappropriate if detailing's effects changed over time or differed across manufacturers or products. For example, for the first entrants, detailing may have expanded the market, while later entrants' efforts may have focused more on encouraging a doctor to use the specific opioid being detailed, rather than any opioid.[194] This is also inappropriate if the products vary in the extent to which they are substitutable. Long-acting products are closer substitutes to other long-acting products than to short-acting products, for example.[195] Detailing of a long-acting product is unlikely to affect prescriptions of long-acting opioids and short-acting opioids in the same way.

(85) In past litigation, Professor Rosenthal has acknowledged the importance of differentiating promotion for different products and by different manufacturers in the same class, noting that promotion of one product has a positive effect on that products' volume and a negative effect on competitor volume. For that reason, she included separate measures for different manufacturers' promotion in those models (which she failed to do here).

(Cambridge, MA: The MIT Press, 2003).

192 *See* Rosenthal Rep. ¶ 34.

193 Compounding these issues described above, Professor Rosenthal also inappropriately attributes products to Allergan in some time periods. For example, she inappropriately assigns Anexsia to Allergan. See Rosenthal Rep. Table C.6.

194 *See* Ernst R. Berndt, Linda Bui et al., "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *American Economic Review* 85, no. 2 (1995), 100–105.

195 *See e.g.*, Federal Trade Commission, "Analysis of the Agreement Containing Consent Order to Aid Public Comment," *In the Matter of King Pharmaceuticals, Inc. and Alpharma Inc*., December 29, 2009; Respondent Impax Laboratories, Inc.'s Replies to Complaint Counsel's Proposed Findings of Fact and Conclusions of Law, *In the Matter of: IMPAX LABORATORIES, INC*., February 13, 2018; ALLERGAN_MDL_00044009 at -4009–4021; PPLPC030000994661 at sheet Past 10 Yr Pdts Launch Aligned.

> The key explanatory variables include the level of spending on promotion, both for Zyprexa and for the other atypical antipsychotics with which it competes, the prices for Zyprexa and its competitors, as well as other market events including the entry date of specific competitive atypical antipsychotics and the FDA warning in late 2003…Based on economic theory and evidence reviewed above, my central hypothesis is that, all else equal, Zyprexa's own marketing expenditures will increase quantities sold while competitors' marketing expenditures will decrease quantities sold of Zyprexa.[196]

(86) An important weakness of aggregate models such as those adopted here by Professor Rosenthal is that in using only variation over time in promotion and prescribing, estimation of manufacturer-specific detailing effects is challenging, if not impossible. In statistical terms, the model has too few degrees of freedom. It is preferable to start with a disaggregated model that exploits variation over time as well as across geography and/or products to test the assumption that manufacturers' promotional efforts have identical effects. Professor Rosenthal fails to use the available disaggregated data on detailing and prescribing, such as by geography, manufacturer, product, and prescriber, to validate her assumptions. The literature also suggests that aggregate models yield different results from those that examine manufacturers separately. One study of pharmaceutical marketing concludes "the parameter estimates of the individual brand-level models are so different that pooling across brands, even within the same category, is inappropriate."[197]

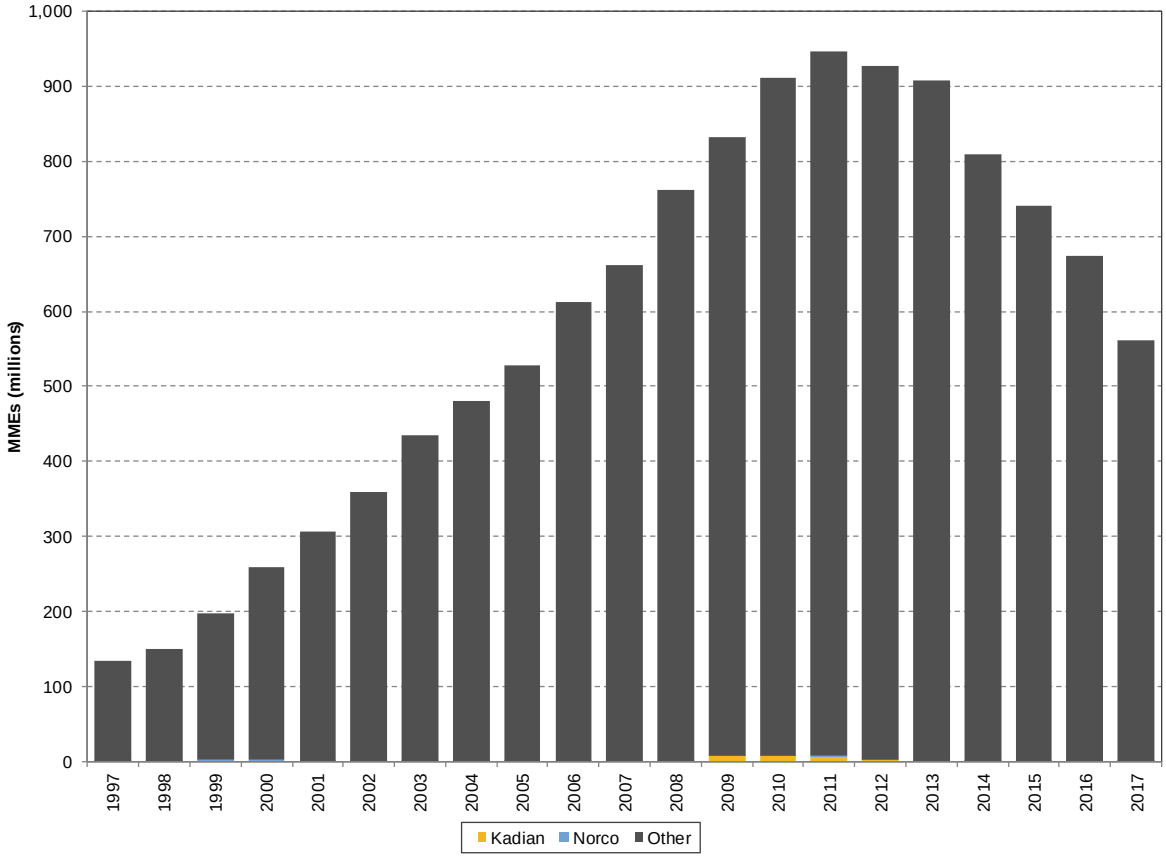
IV.B. The expansion in opioid prescribing is not explained by prescribing of Allergan's products

(87) The scale and timing of Allergan product prescribing is inconsistent with Allergan promotion having contributed to an increase in overall opioid prescribing. The bars in Figure 12–Figure 14 show opioid MMEs dispensed annually from 1997–2017, segmented between Kadian and Norco and all other opioid products. I include separate figures for Cuyahoga and Summit counties and for the entire United States. In both these two counties and nationally, MMEs increase steadily from 1997 through 2010, peak in 2011, and decline thereafter. MMEs associated with Allergan products, shown in yellow for Kadian and blue for Norco at the bottom of the figures, are barely visible.

[196] Exhibit E, Declaration of Meredith Rosenthal, *Hood v. Eli Lilly & Co*, No. 1:07-cv-00645-JBW-RLM, Dkt. 208-4, at 4772 (E.D.N.Y Oct. 9, 2009) ¶ 36–38.

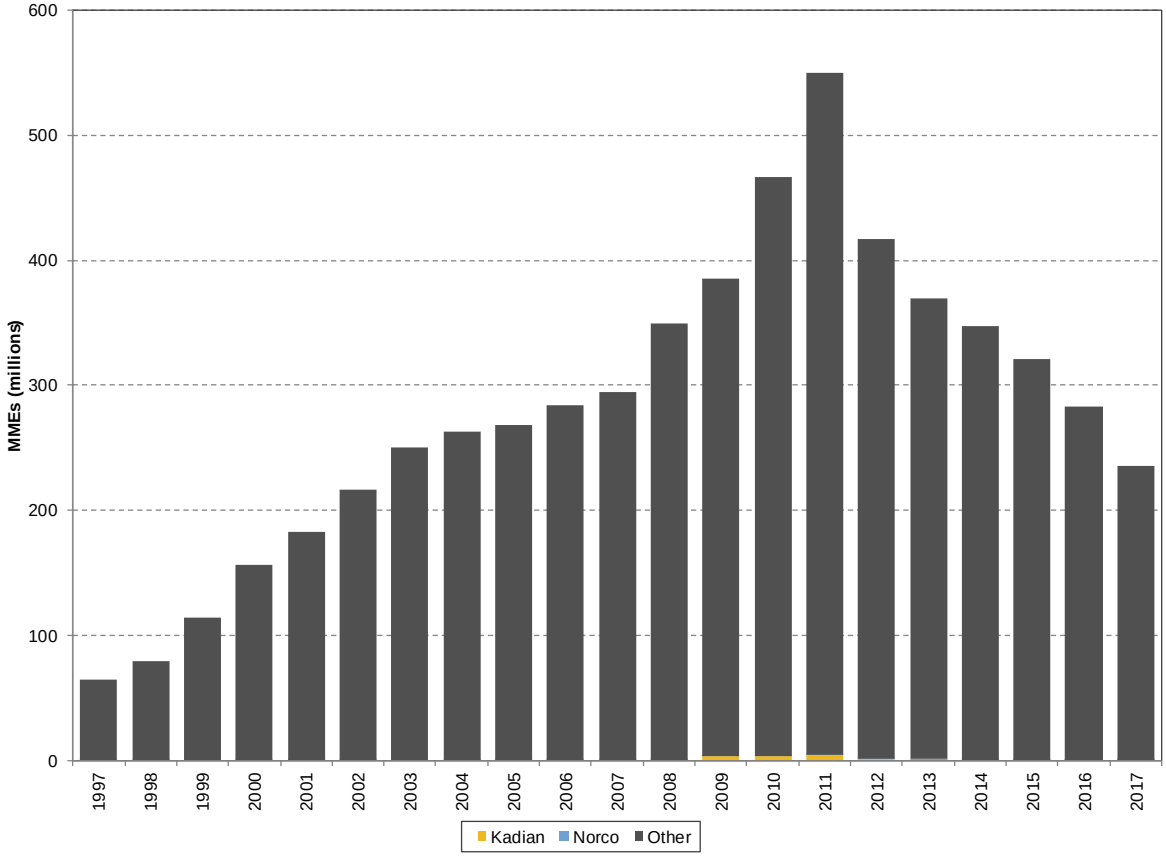
[197] Peter S. H. Lieflang and Jaap E. Wieringa, "Modeling the Effects of Pharmaceutical Marketing," *Marketing Letters* 21, no. 2 (2010), 131.

Figure 12: MMEs prescribed in Cuyahoga County for Kadian and Norco and all other opioid products, by year



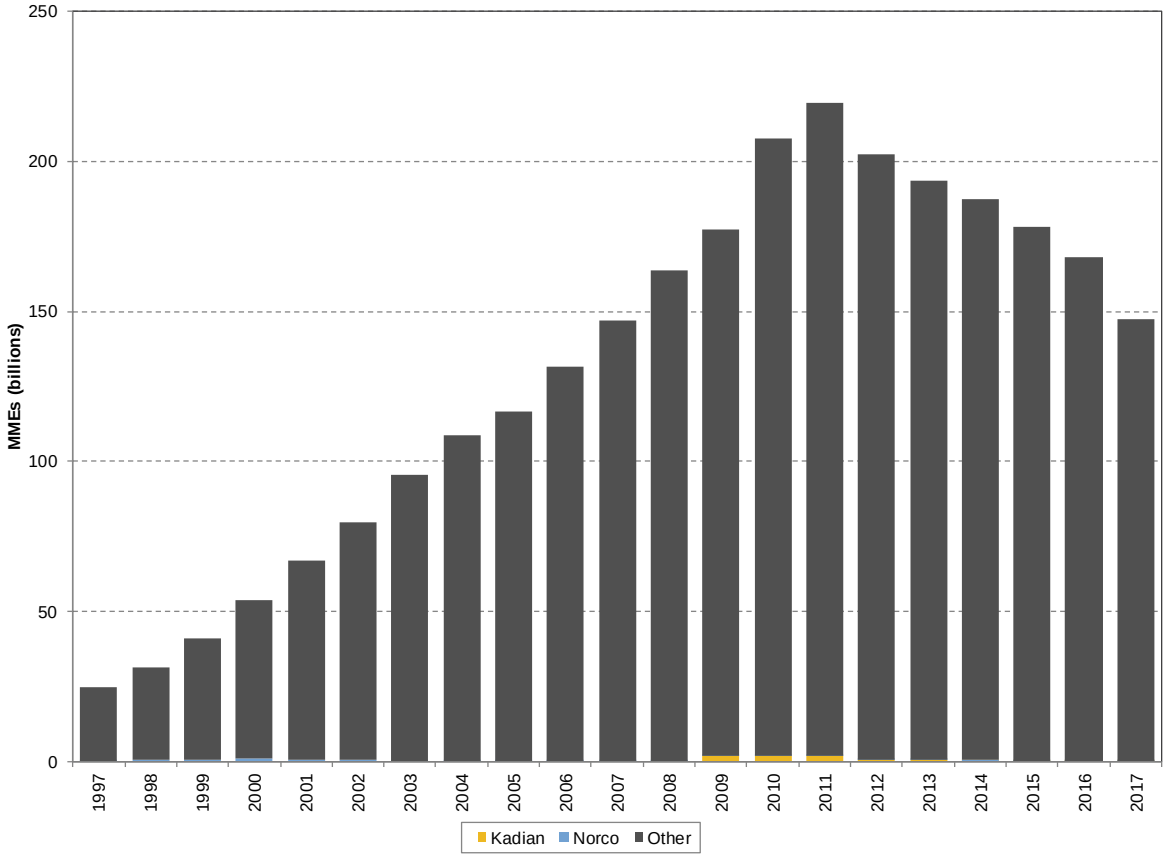
Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data; prescription to MME conversion factors obtained from CDC.

Figure 13: MMEs prescribed in Summit County for Kadian and Norco and all other opioid products, by year



Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data; prescription to MME conversion factors obtained from CDC.

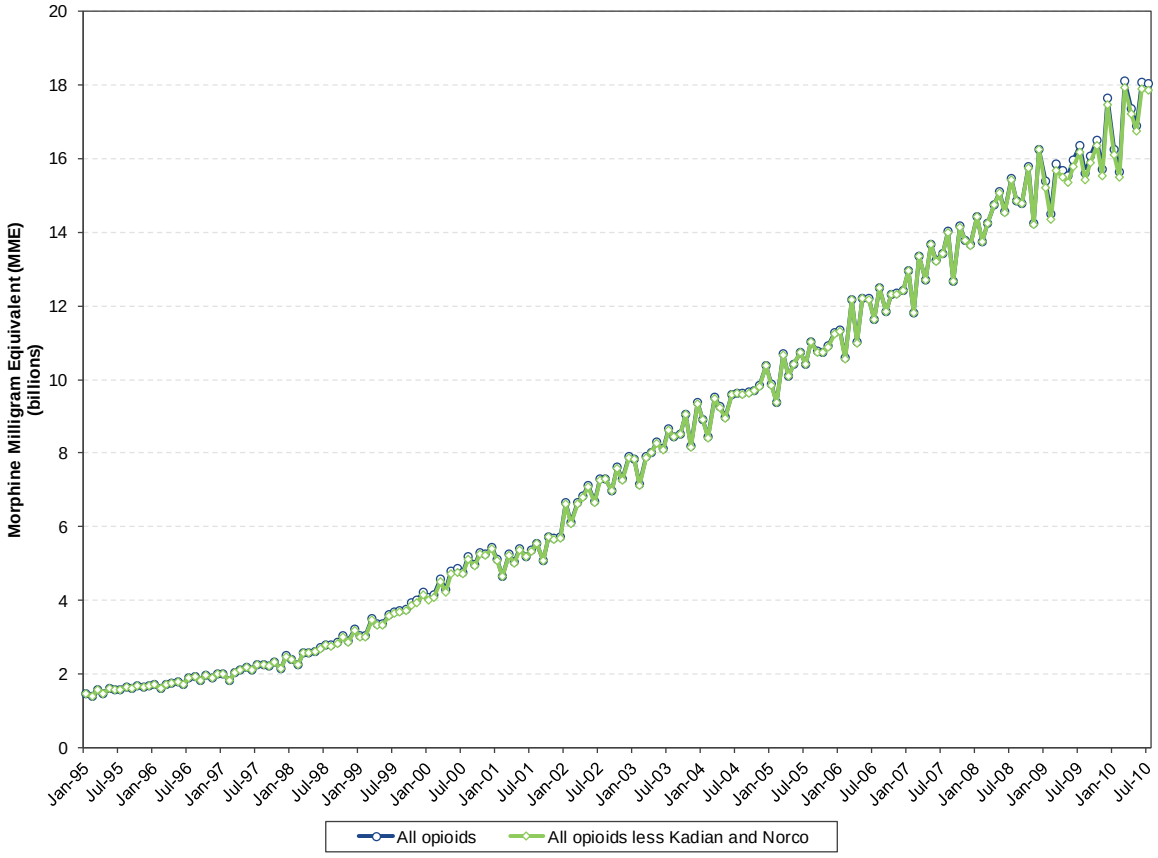
Figure 14: MMEs prescribed nationally for Kadian and Norco and all other opioid products, by year



Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data; prescription to MME conversion factors obtained from CDC.

(88) In Figure 15, I graph the increase in MME sales during the first and second era as identified by Professor Rosenthal in her direct model, and I compare that increase in total opioid MMEs to the MMEs that would have occurred assuming no prescribing of Allergan products. The two lines in Figure 15 are virtually indistinguishable, with no noticeable change in the trend of opioid MMEs as Allergan products are included or excluded. This suggests that Allergan's promotion did not materially change the opioid market.

Figure 15: The overall increase in opioid MMEs during Professor Rosenthal's first and second eras, with and without Kadian and Norco MMEs



Source: Rosenthal backup data.

(89) The timing of reductions in the prescribing of Allergan's products is also inconsistent with the periods of aggregate increases in opioid prescribing. For example:

- Norco monthly MMEs began declining in June 2000, and they declined by 68% through February 2001. Over the same period, overall opioid MMEs *increased* by 8%.
- Kadian monthly MMEs began declining soon after Allergan's acquisition of the product in December 2008, and MMEs declined by 21% through October 2011. Over the same period, overall opioid MMEs *increased* by 28%.

The increases in total opioid MMEs during these periods indicates that the market expanded because of the increased prescribing of *other* opioid products while Allergan's detailing decreased. Thus, Plaintiffs' experts have demonstrated no causal link between Allergan's promotion and the opioid prescribing increases that occurred as prescribing declined for Allergan's products.

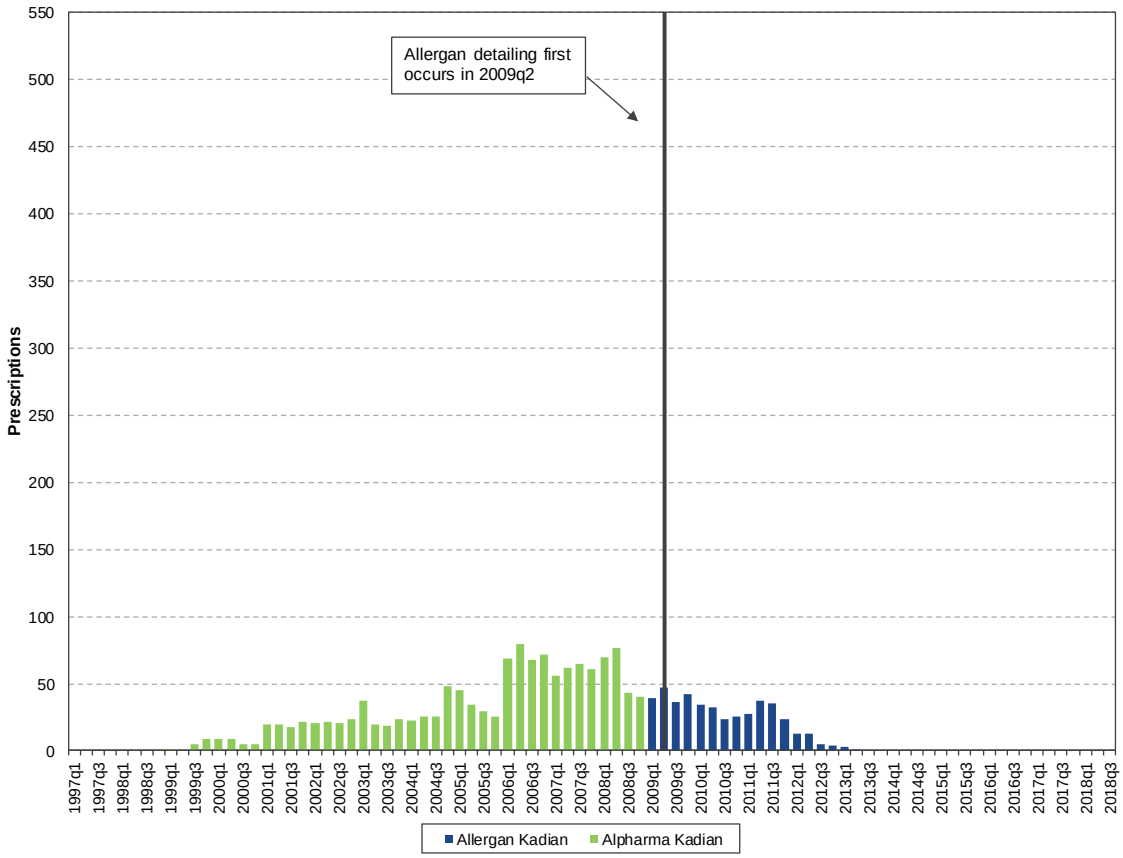
IV.C. Provider-level Kadian prescribing patterns corroborate that Allergan did not expand opioid prescribing

(90) In contrast to Plaintiffs' economic experts, who only analyze opioid prescribing and shipments in the aggregate and admittedly have not analyzed how specific doctors were affected by detailing,[198] I examine how the Kadian prescribing of individual providers in Cuyahoga and Summit counties responded to Allergan promotion. I focus on Kadian prescribing for two reasons: (1) Plaintiffs' allegations and the documents cited by Plaintiffs' experts are almost entirely limited to Kadian and (2) data on Allergan detailing is available only for Kadian. With these data, I identify 45 prescribers in Cuyahoga or Summit counties whom Allergan detailed with respect to Kadian, and I am able to link 41 of them to the corresponding monthly prescribing I observe in the IMS/IQVIA Xponent and PlanTrak data.

(91) For each of these 41 prescribers, I analyze how the number of Kadian prescriptions they wrote changed after Allergan acquired the product from Alpharma and first detailed them. For example, in Figure 16 I show the quarterly number of Kadian prescriptions written by Dr. Teresa Dews, who practices in Cuyahoga County. The green bars represent the number of Kadian prescriptions Dr. Dews wrote prior to Allergan acquiring the product. Allergan detailed Dr. Dews shortly after it acquired Kadian, yet the amount of her Kadian prescribing declined thereafter. The blue bars represent Allergan's Kadian, and the vertical black line identifies the quarter in which the first Allergan detail occurred for this prescriber. Similar examples appear in Figure 17 and Figure 18.

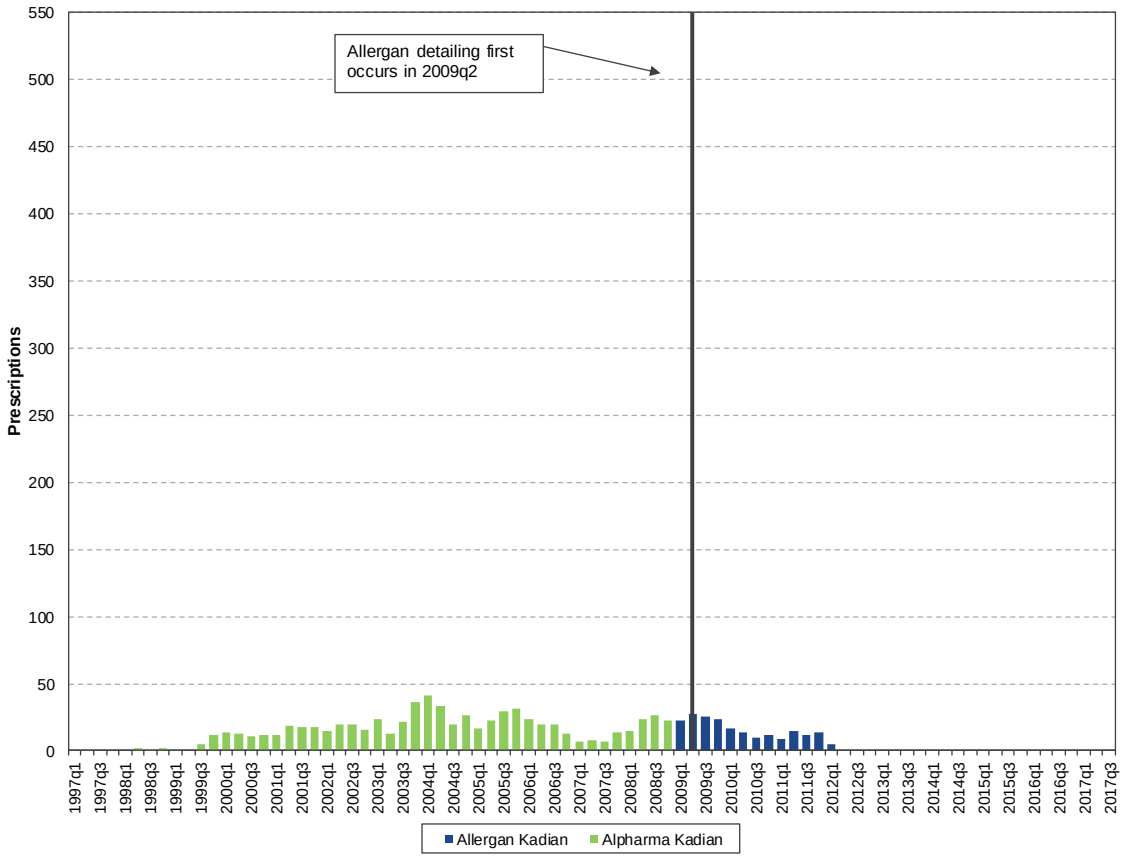
[198] Rosenthal May 4 Dep. at 97:13–97:24.

Figure 16: Dr. Teresa Dews's Kadian prescribing



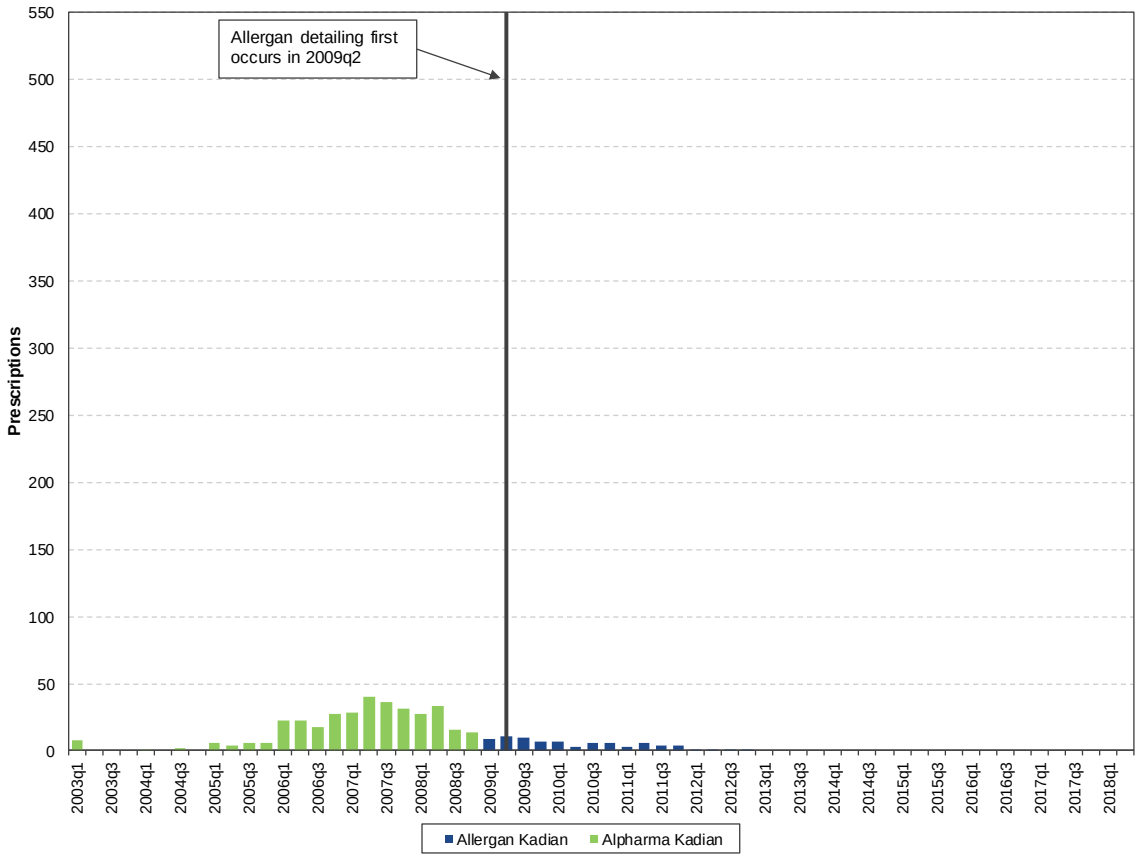
Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data; Allergan call notes.

Figure 17: Dr. Dan Shamir's Kadian prescribing



Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data; Allergan call notes.

Figure 18: Dr. Priti Nair's Kadian prescribing



Source: IQVIA Xponent (1997–2007) and PlanTrak (2008–Apr 2018) data; Allergan call notes.

(92) Of the 41 Cuyahoga or Summit County prescribers Allegan detailed with respect to Kadian:

- 10 prescribed no Kadian after the first Allergan detail.
- 12 prescribed no more than 16 Kadian prescriptions in any quarter after the first Allergan detail, or less than 1.25 per week.
- 17 exhibit no material increase in their Kadian prescribing trend after the first Allergan detail, and of these, 7 exhibit a declining Kadian prescribing trend after the first Allergan detail.
- The remaining 2 prescribers' Kadian prescribing increased, but their Kadian prescribing as a share of all of their respective opioid prescribing remained relatively constant until declining in 2012.[199]

[199] [redacted]

(93) For 39 of the 41 prescribers in Cuyahoga and Summit counties detailed by Allergan, they either prescribed no or very few Kadian prescriptions thereafter, or they continued or reduced their levels of Kadian prescribing relative to the levels prior to any Allergan detailing. These patterns are consistent with the substitution and maintenance objectives reflected in Allergan's promotional materials. These patterns are also consistent with the messaging of the corrective action that represents 85% of the promotional activity by Allergan for Kadian, which included highlighting potential risks of opioids and was unlikely to expand the market for either Kadian or opioids more generally. Professor Rosenthal testified that she included corrective detailing in her model and assumed it was unlawful.[200]

IV.D. Allergan Kadian prescribing patterns across patients are inconsistent with Plaintiffs' allegations that Allergan promotion is unlawful and market expanding

(94) By employing aggregate models in which the effects of all marketing and prescribing is assumed to have been identical, Plaintiffs' economic experts ignore available prescriber- and patient-level data that would shed light on the differences in the nature and effectiveness of promotion for different manufacturers, products, or time periods, as well as differences in the likelihood that certain marketing and prescribing would have led to harms. Professor Cutler acknowledges the value of such data, but incorrectly asserts that such data are not available. He states:

> Moreover, available data on shipments are defined on the basis of morphine equivalents (MMEs) per capita. While this provides a comprehensive measure of shipments of prescription opioids measured on an 'apples to apples' basis, it does not permit the evaluation of prescription-level characteristics that also may affect misuse and mortality. For example, available data do not permit analysis of the impact on mortality of factors such as the average number of days for which prescriptions are written, whether the prescribed drug was long acting or extended release formula, or the average dosage prescribed per day. Each of these is likely to affect the relationship between shipments and addiction, crime, mortality, and other outcomes.[201]

In this section I explain that the patterns of prescribing associated with prescribers from Cuyahoga and Summit counties who received Allergan Kadian detailing is inconsistent with Plaintiffs' allegations that Allergan promotion is unlawful and market expanding. By exploring patient-level

[200] Rosenthal May 4 Dep. at 217:20–218:14.

[201] Cutler Rep. ¶ 75. Professor Cutler predicts that "this type of mismeasurement problem would also be expected to lead to an underestimate of the true relationship between consumption and mortality" but ignores the fact that the omitted variable bias could instead *overestimate* the relationship between consumption and mortality, whether with respect to all opioids or Allergan's products specifically.

prescribing patterns for these providers, I am able to demonstrate that Allergan's alleged promotion did not lead to improper prescribing.[202]

(95) [redacted]

[redacted]

(96) [redacted]

[redacted]

[redacted]

(97) [redacted]

[203] I am also conservative in that I do not identify Alpharma Kadian as a prior opioid. Thus, my percentages in Figure 20 would not include any patients who took only Apharma Kadian before transitioning to Allergan Kadian. I explain in the previous section that the Cuyahoga and Summit county prescribers detailed by Allergan with respect to Kadian routinely either maintained or reduced their level of Kadian prescribing after being detailed by Allergan.

[redacted]

[redacted]

[redacted]

[204] I have excluded outliers for this analysis, which I defined as patients outside 1.5 times the interquartile range for each provider, as is standard practice for box and whisker plots.

Source: Ohio Automated Rx Reporting System (OARRS) data.

(99) [redacted]

[redacted]

[205] U.S. Food and Drug Administration, "Kadian drug label." Allergan USA, Inc. (2018), available athttps://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020616s061s062lbl.pdf.

(100) A contemporaneous national interview of prescribers detailed by Allergan corroborates the importance of patient-specific factors in their decision to prescribe Kadian:[206]

- "You're mainly looking at what patient experiences have been in the past…usually mechanical, orthopedic, neuropathic pain will require a long acting opioid. I don't think there is a specific

[206] The survey presentation notes: "In-depth, blinded telephone interviews were conducted with twelve (12) high-volume prescribers of long-acting opioids to understand:
- The position of KADIAN in the minds of prescribers within the competitive environment
- Drivers of therapeutic selection within the long acting opioid category
- Profile of the KADIAN patient by dosage strength vs. competitors
- "Ideal" range of dosage strengths
- Future trends in pain management/therapeutic development.

Interviewees were randomly recruited from a target list provided by Actavis." ALLERGAN_MDL_00761198 at -1204.

product by indication, I don't think that I prescribe based on type or severity of pain. Age, history with pain meds and formulary are real drivers to selection."[207]

- "The research is not solid enough to pick one molecule over another. Formulary and history of what has worked with a patient previously are the drivers. An inverse drive is the desirability of a drug on the street. Kadian is the least desired followed by Opana and Oxycontin."[208]

(101) Consistent with my analysis of the Cuyahoga and Summit prescribers, those interviews also confirm that when Allergan's detailing targets prescribed Kadian, they typically relied on doses of 100 MMEs per day or less, but varied their dosages to meet the needs of patients[209]:

- "The wide range of doses allow us to fine tune or make adjustments for every 12 or 24 hours"[210]
- "Can start with a low dose which is especially relevant with the elderly"[211]
- "The dosing is a benefit with Kadian, I think they have every dose known to man available. Small doses make it easier to figure out the dosing as you can make small doses vs. jumping up with bigger ones."[212]
- "Most common Kadian dosing is 20, 30, 50mg which is 80% overall and I might use 10mg about 10% of the time, I have 1 patient on 100mg."[213]

(102) Moreover, as Professor Cutler has admitted, the analyses offered by Plaintiffs' economic experts "[do] not permit the evaluation of prescription-level characteristics that also may affect misuse and mortality."[214] Relative price is one key factor that should be considered in assessing the likelihood of a drug leading to misuse and mortality. Plaintiffs' expert Professor Gruber explains in his report that individuals who misuse prescription opioids are cost-sensitive and turn to lower priced products, and Plaintiffs' expert Professor Rosenthal finds in her model that higher prices reduce consumption.[215] Another of Plaintiffs' experts, Dr. Katherine Keyes, explains in her report:

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207 ALLERGAN_MDL_00761198 at -1204.

208 ALLERGAN_MDL_00761198 at -1206.

209 "Nearly all respondents" reported "commonly used dosage strength[s]" of 10mg, 20mg, 30mg, and 50mg. Because Kadian can be prescribed in dosages of one or two pills per day, this translates to MMEs per day ranging from 10 to 100. "More than half of respondents" also reported dosages of 60mg and 100mg, and "Very few/None" reported dosages of 80mg and 200mg. ALLERGAN_MDL_00761198 at -1209.

210 ALLERGAN_MDL_00761198 at -1206.

211 ALLERGAN_MDL_00761198 at -1206.

212 ALLERGAN_MDL_00761198 at -1206.

213 ALLERGAN_MDL_00761198 at -1210.

214 Cutler Rep. ¶ 75.

215 Professor Gruber explains this in the context of individuals shifting from higher priced opioids to lower-priced illicit products, but the same price sensitivity would cause individuals to shift from higher priced prescription opioids to lower priced prescription opioids. "Effectively, a variety of elements of public policy and the legal environment raised the relative costs of using prescription opioids, leading those individuals who had become addicted to prescription opioids

> Indeed, there are decades of public health research that have a strong analogy to the current opioid epidemic. The relationship between supply of an addictive substance and subsequent rates of substance use disorder has been well established in the public health literature for years, under the model of "availability theory". Succinctly, this theory posits that one driver of population burden related to substance use harm is the availability and cost of the substance. **The relationship between availability/cost and harm has been extensively documented for decades** for alcohol and tobacco, and is one reason that alcohol and **cigarette taxes, minimum pricing, and other public health efforts aimed at availability and price are among the most effective population level interventions** to reduce alcohol-related harms such as alcohol-impaired driving fatalities.[216]

Plaintiffs' expert Professor Rosenthal also acknowledges the importance of price and competitor pricing when evaluating prescription volume, and has demonstrated this empirically in past litigation.

> The findings are consistent both with economic theory and previous studies. That is, the effect of Zyprexa's own price is negative while the prices of competitor drugs have a positive relationship to Zyprexa sales.[217]

(103) I evaluate how the price of Kadian and Norco compare to selected generic opioids. In Figure 24, I demonstrate that generic extended-release morphine, generic oxycodone, and generic hydrocodone APAP would yield savings per prescription relative to Kadian ranging from 81%–94%. Those generics would yield savings per prescription relative to Norco ranging from 6%–72%. The substantially lower prices of generic opioid products would likely discourage most cash-paying customers from using Kadian or Norco, and out-of-pocket expenditures for insured individuals would often be significantly lower for generic opioids than for Kadian and Norco.

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to turn to substitute products to satisfy that addiction." Gruber Rep. ¶ 51;

"As intake increased, coupled with the cost of prescription opioids and availability (and post-2010 pills being more tamper resistant), many participants turned to heroin. Nearly all the participants who turned to heroin reported the cost savings as the primary motivation." Gruber Rep. ¶ 93.

"The price index, with a coefficient of −7,689,846,168, is statistically significant and in the expected direction (higher prices lead to lower MMEs)," Rosenthal Rep. ¶ 70.

[216] Keyes Rep. p. 29.

[217] Exhibit E, Declaration of Meredith Rosenthal, *Hood v. Eli Lilly & Co*, No. 1:07-cv-00645-JBW-RLM, Dkt. 208-4, at 4772 (E.D.N.Y Oct. 9, 2009) ¶ 43.

Figure 24: Average retail savings of generic opioids relative to Kadian and Norco, per Rx

Generic product	Kadian	Norco
Morphine Sulfate ER	81%	6%
Oxycodone	91%	55%
Hydrocodone APAP	94%	72%

Source: Rosenthal backup data

V. Plaintiffs' experts have failed to demonstrate a link between Allergan's detailing and harm

(104) None of Plaintiffs' experts directly tests the key links between promotion and shipments or promotion and harm despite the availability of dispositive data. Instead, Professor Rosenthal assesses the link between *national* opioid detailing and *national* opioid prescription-based MMEs, which may be misleading about the extent to which county-level detailing caused county-level opioid prescribing, opioid shipments, or opioid-related harms. Professor Rosenthal's indirect model is her only attempt at examining county-level variation, in which she assumes (rather than tests) that all unexplained county-level variation in opioid shipments must be caused by manufacturer conduct. A direct assessment of this link reveals that Allergan county-level detailing does not explain county-level variation in opioid shipments or county-level opioid mortality.

V.A. Plaintiffs' expert economists neglect to evaluate whether manufacturer promotion explains county-level variation in opioid shipments or harm

(105) Professor Rosenthal's direct model, which feeds into Professor Cutler's model and ultimately into Professor McGuire's damage calculations, examines the link between national opioid detailing and national opioid prescribing. Professor Cutler assesses the link between county-level opioid shipments and county-level opioid mortality and crime. Neither expert directly assesses the critical links in the causal chain regarding the extent to which county-level detailing causes county-level shipments or opioid-related harms.

(106) Professor Rosenthal's indirect model, which does not contribute to Professor McGuire's final damage calculations, is her only assessment of county-level variation. Professor Rosenthal assumes that all county-level variation in opioid shipments must be a result of manufacturer conduct if it is not otherwise accounted for by a limited set of demographic and economic characteristics. She does not directly assess whether county-level variation in opioid shipments is explained by manufacturer conduct despite the availability of data to do so. Further, Professor Rosenthal's conclusion that manufacturer conduct caused county-level variation in opioid shipments is inconsistent with statements in depositions and in her own report that indicate that marketing campaigns are national (e.g., the marketing message does not vary by geography, and physician targets are selected based on prescription volume rather than geography). Marketing is therefore unlikely to be an important driver of geographic variation.

(107) In the context of his own indirect model, Professor Cutler explains that indirect models are "useful when the independent variable one wishes to measure is unavailable or is measured only with

error."[218] But Professor Rosenthal has access to robust detailing data that can be mapped to the county level, at a minimum for Allergan's Kadian, such that her indirect model is not warranted. Professor Cutler also concedes that "[t]he indirect regression attributes the entirety of unexplained opioid-related mortality to shipments. To the extent that other factors not modelled in the "baseline" regression contributed to increases in opioid mortality, the indirect approach has the potential to overstate the impact of defendants' actions."[219]

(108) The same potential overstatement of the impact of defendants' actions applies to Professor Rosenthal's indirect model, in which she attributes all unexplained opioid shipments to manufacturer conduct, including defendants and non-defendants. Professor Rosenthal also agrees that omitting factors that explain variation in county-level shipments could overstate the impact of promotion on shipments, but she attributes the majority of county-level variation in shipments to manufacturer conduct (i.e., 67% across all years) without providing any direct evidence that promotion has any correlation with county opioid shipments.[220] Further, she omits other key variables that might explain the geographic variability in opioid shipments, such as pill mills and illegal prescribing, which would lead to the overstatement of the impact of defendants' actions cautioned against by Professor Cutler.[221] Professor Rosenthal acknowledges that her indirect model omits a number of potentially relevant factors, but she argues without any supporting analysis that she believes that the effects of many of these factors would be picked up by variables included in her model.[222] I discuss these omissions further in Section VI.C.

V.B. Kadian detailing explains essentially none of the county-level variation in opioid shipments or opioid deaths

(109) I use the available prescriber-level Kadian detailing data to directly assess the link between county-level variation in detailing and county-level variation in opioid shipments.[223] In Figure 25, I demonstrate that counties with more opioid shipments do not have more Allergan Kadian details. The top panel arrays the 404 counties included in Professor Cutler's analysis based upon their 2010 opioid shipments per capita per day, with the county with the fewest opioid shipments on the left and the county with the most opioid shipments on the right. The bottom panel arrays Kadian details by county in 2010, with the ordering of counties maintained from the top panel. If Kadian detailing explains the county-level variation in opioid shipments, I would expect to observe that counties with more opioid

[218] Cutler Rep. ¶ 80.

[219] Cutler Rep. footnote 53.

[220] Deposition of Professor Meredith Rosenthal, May 5, 2019 [hereinafter "Rosenthal May 5 Dep."] at 586:21–587:8.

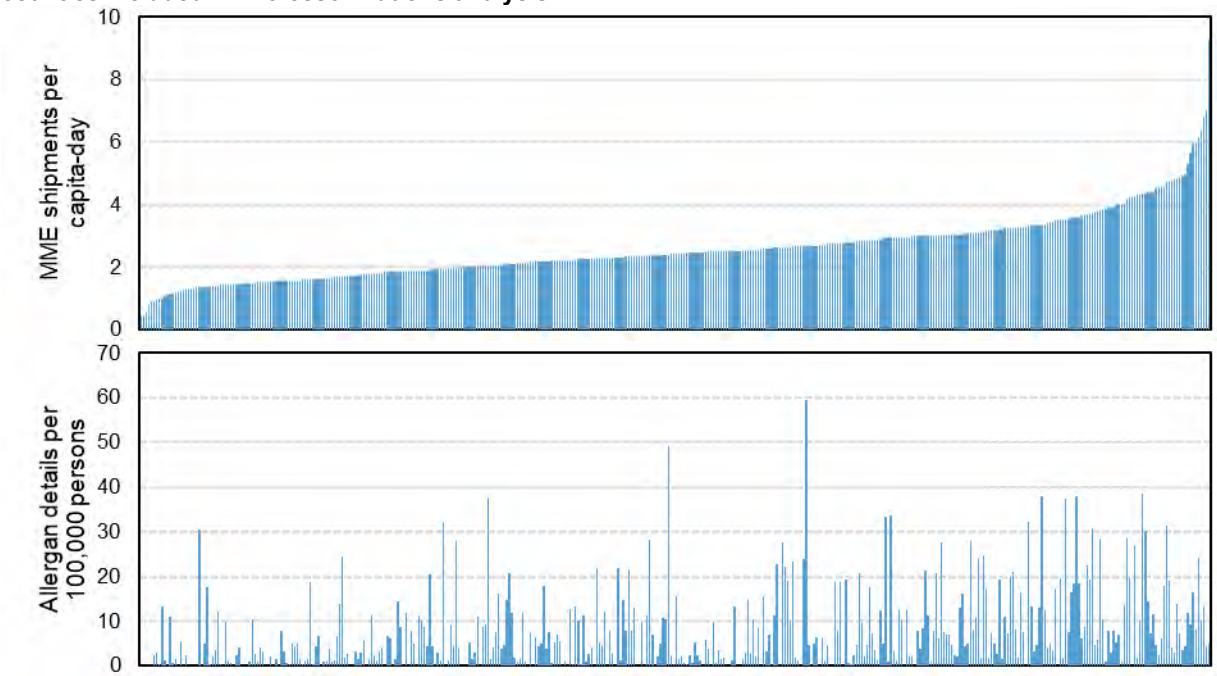
[221] Professor Rosenthal agrees that she did not include in her indirect model factors such as the count of pill mills in a county or "the existence or volume of illegal prescribing in the county." *See* Rosenthal May 5 Dep. at 593:2–595:14.

[222] *See e.g.* Rosenthal May 5 Dep. at 587:10–592:25.

[223] I used prescriber zip codes in the detailing data to map details to counties.

shipments also have more Kadian details. However, counties with the most MMEs (at the far right) have roughly average levels of Kadian detailing in the lower panel; the county with the highest number of details is only slightly above the median number of MMEs. Importantly, the lack of relationship between Kadian detailing and shipments breaks the causal chain that is the basis of the collective opinions of Professors Rosenthal, Cutler, and McGuire.

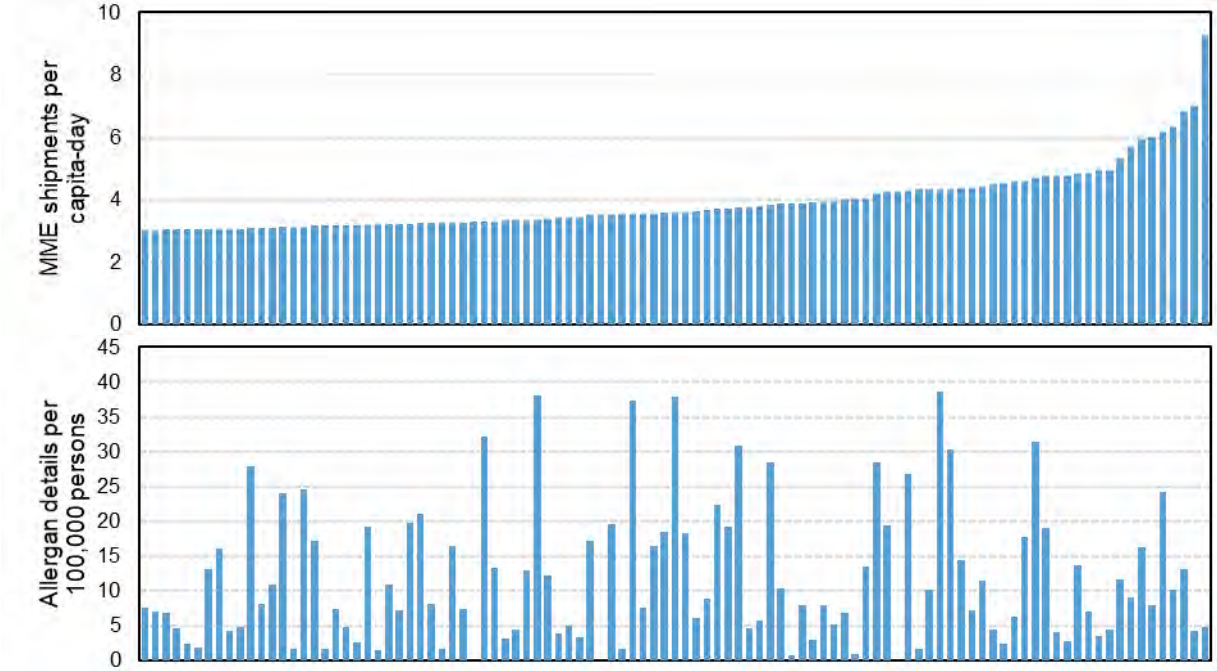
Figure 25: 2010 county-level variation in opioid shipments and Allergan detailing for the 404 large counties included in Professor Cutler's analysis



Source: Professor Cutler mortality and demographic data; Allergan call notes; Quarter 2014 Zip-County USPS Crosswalk

(110) In Figure 26, I provide the same information as in Figure 25 except limited to the top quartile of counties in terms of opioid shipments, where risk of harm is greatest. This figure provides a closer look at the relationship between opioid shipments and Allergan details, and it shows that among the top quartile of counties in terms of opioid shipments, there is no relationship between the level of Kadian detailing and opioid shipments.

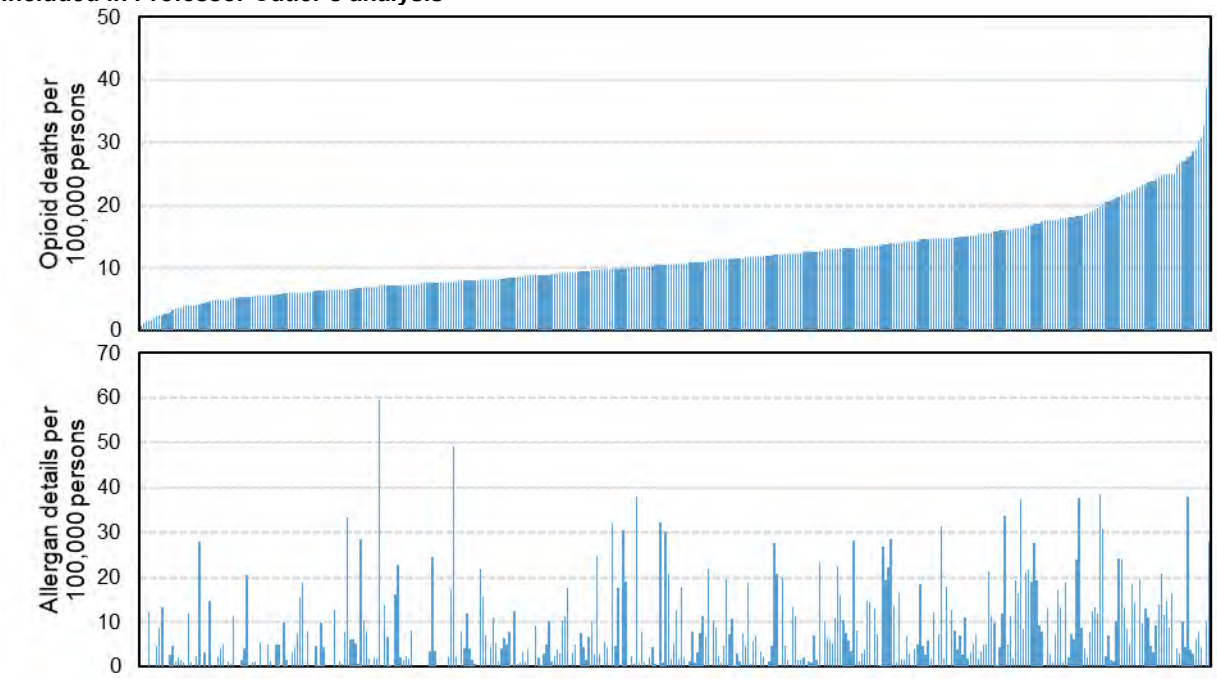
Figure 26: 2010 county-level variation in opioid shipments and Allergan detailing for large counties in top quartile of opioid shipments



Source: Professor Rosenthal shipment and demographic data; Allergan call notes; Quarter 2014 Zip-County USPS Crosswalk

(111) I also directly assessed the relationship between Kadian detailing and opioid mortality that Plaintiffs' experts neglected to measure. In Figure 27, I array opioid deaths per 100,000 persons in 2010 for each of the 404 counties included in Professor Cutler's analysis, with the county with the fewest opioid deaths on the left and the county with the most opioid deaths on the right. The bottom panel arrays Kadian details by county in 2010, with the ordering of counties maintained from the top panel. If Kadian detailing explains the county-level variation in opioid deaths, I would expect to observe that counties with more opioid deaths also have more Kadian details. Once again, there is no relationship between the level of Kadian detailing and opioid-related mortality. Importantly, the lack of relationship between Kadian detailing and opioid deaths provides direct evidence against Plaintiffs' causal chain.

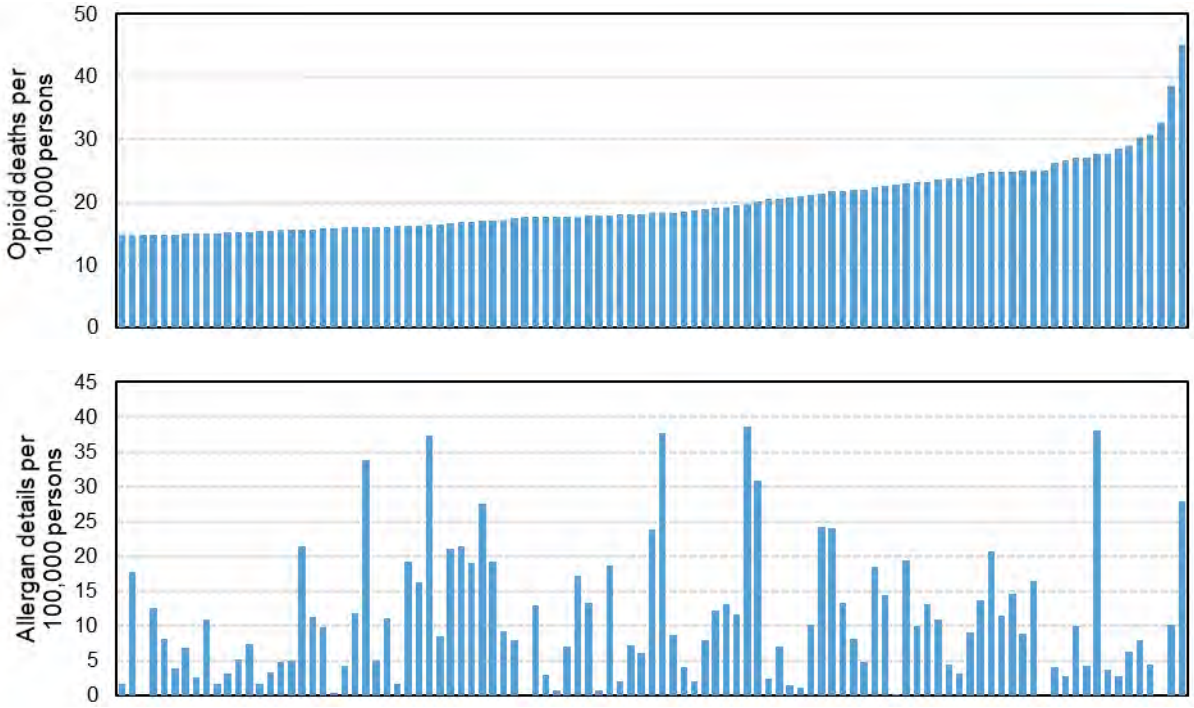
Figure 27: 2010 county-level variation in opioid mortality and Allergan detailing for the 404 large counties included in Professor Cutler's analysis



Source: Professor Cutler mortality and demographic data; Allergan call notes; Quarter 2014 Zip-County USPS Crosswalk

(112) In Figure 28, I provide the same information as in Figure 27 except limited to the top quartile of counties in terms of opioid deaths. This figure provides a closer look at the relationship between opioid deaths and Allergan details, and it shows that among the top quartile of counties in terms of opioid deaths, there is no relationship between the level of Kadian detailing and opioid-related mortality.

Figure 28: 2010 county-level variation in opioid mortality and Allergan detailing for large counties in top quartile of opioid deaths



Source: Professor Rosenthal shipment and demographic data; Allergan call notes; Quarter 2014 Zip-County USPS Crosswalk

(113) Although the lack of a correlation between Kadian detailing and all opioid shipments and between Kadian detailing and opioid deaths is visually evident in Figure 25–Figure 28, I corroborate these findings econometrically. Specifically, I perform two regression analyses. The first assesses the relationship between Kadian detailing contacts and all opioid shipments (as measured in MMEs per capita per day) and the second assesses the relationship between Kadian detailing contacts and opioid deaths per 100,000 persons. Both models analyze the respective relationships over the course of four years (2009–2012) in the 404 large counties analyzed by Professors Rosenthal and Cutler. Consistent with Figure 25–Figure 28, I find that there is no evidence of a relationship between Kadian details and opioid shipments or between Kadian details and opioid deaths. These results are robust to a variety of model specifications.[224]

[224] I assess the relationship between county-level Kadian details per capita per day on county-level opioid shipments and opioid mortality using three detailing sensitivities: (1) annual flow, (2) cumulative stock with 0% annual depreciation, and (3) depreciated stock with 5% annual depreciation. I include yearly dummies to account for changes in opioid shipments and opioid deaths over time, along with the same county-level demographics included in Professor Rosenthal's indirect regression. I test sensitivities with and without a first-differences approach to account for potential non-stationarity.

V.C. Professor Cutler's relationship between opioid shipments and harms is therefore disconnected from Kadian detailing

(114) Professor Cutler's exercise of linking opioid shipments to county-level harm in order to conclude that manufacturer promotion caused that harm is contingent upon Plaintiffs' unestablished link between manufacturer promotion and opioid shipments. Neither Professor Cutler nor Professor Rosenthal directly assesses this link, which my Allergan-specific models soundly reject. Kadian detailing does not explain opioid shipments or opioid deaths, so the opioid-related harms measured by Professor Cutler cannot be attributed to Allergan's promotion.

VI. Plaintiffs' experts' models are flawed and unreliable

(115) Though the majority of my report focuses on the failure of Plaintiffs' economic experts to demonstrate that Allergan promotion caused the harms they analyzed, their models also suffer from numerous conceptual and mechanical errors that render them incapable of demonstrating a causal relationship between defendant promotion and harm more generally. In this section I outline some of those flaws as follows:

- In Section VI.A, I demonstrate that Professor Rosenthal's direct causation model deviates from the literature and violates basic economic principles, which causes her preferred model to manufacture a nearly perfect relationship between detailing and prescription MMEs. Correcting for this grave econometric error effectively eliminates the estimated impact of manufacturer promotion.
- In Section VI.B, I explain that Professor Rosenthal's direct causation model is a goal-seeking exercise that assumes its conclusion, and is thus incapable of measuring a causal relationship between defendant promotion and opioid prescribing. She purports to rely on standard econometric approaches, but she makes unsupported assumptions and obtains results that are contrary to economic theory and to common sense.
- In Section VI.C, I explain that Professor Rosenthal's direct and indirect models both fail to consider a multitude of other factors that potentially explain opioid MMEs. Professor Rosenthal has previously described the inclusion of confounding factors as a "condition for valid causal inference" that are "highly problematic" if not considered.[225]
- In Section VI.D, I explain that Professor Rosenthal's "under-treated pain" analysis may ignore clinically appropriate uses of opioids.
- In Section VI.E, I describe Professors Cutler's and Gruber's failure to consider alternative explanations for the increase in opioid-related harm, a flaw Professor Cutler acknowledges "has the potential to overstate the impact of defendants' actions."
- In Section VI.F, I assess the extent to which prescription MMEs, rather than shipments, explain the county-level variation in mortality that Professor Cutler observes. I find that prescription MMEs, which are the basis of Professor Rosenthal's preferred model and are a more direct reflection of manufacturer promotional efforts than shipments, reduce his damages estimate by nearly half.
- In Section VI.G, I explain that Plaintiffs' combined damages framework, which multiplies a long chain of unrelated estimates, fails to consider any measure of error and omits critical pieces of the

[225] Declaration of Meredith Rosenthal, *In re Neurontin Marketing, Sales Practices, and Products Liability Litigation*, MDL Docket No. 1629, Master File No. 04-10981, (D.Ma. September 14, 2006) ¶ 10.

causal chain in such a way as to invalidate any precise dollar amount they purport to measure as harm.

VI.A. Professor Rosenthal's direct causation model violates basic economic principles

(116) Professor Rosenthal's direct model assesses the relationship between promotion and prescribing of MMEs over time using a time series model. Time series modeling is an established econometric approach that, like all regression models, relies on assumptions about the underlying data that must be satisfied in order to produce accurate results. One of these assumptions is that the underlying time series must be "stationary," which means that its mean, variance, and covariance are not a function of time.[226] Importantly, the consequences of violating this assumption, also known as a "unit root" problem, are severe:

> The main reason why it is important to know whether a time series is stationary or nonstationary before one embarks on a regression analysis is that there is a danger of obtaining apparently significant regression results from unrelated data when nonstationary series are used in regression analysis. Such regressions are said to be spurious.[227]

Symptoms of spurious regressions are well established in the econometrics literature and include high R-squareds and highly significant estimated effects. Professor Rosenthal's preferred model R-squared of 99.36% and highly significant detailing stock effects are clearly indicative of the issue described in the literature:

> The possibility of spurious regression with I(1) [non-stationary] variables is quite important and has led economists to reexamine many aggregate time series regressions whose t statistics were very significant and whose R-squareds were extremely high.[228]

Professor Rosenthal is familiar with the stationarity assumption of time series models and the severe consequences of violating this assumption:

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[226] R. Carter Hill and William E. Griffiths, *Principles of Econometrics*, Fourth ed. (Danvers, MA: John Wiley & Sons, 2011), 476.

[227] R. Carter Hill and William E. Griffiths, *Principles of Econometrics*, Fourth ed. (Danvers, MA: John Wiley & Sons, 2011), 482.

[228] Jeffrey M. Woolridge, *Introductory Econometrics: A Modern Approach* (Mason, OH: Thomson South-Western, 2006), 647.

- Q. And do you agree that when there's a slow-moving trend in one variable through time, it is very difficult to infer its causal effect on another variable?

  A. I believe that you're describing again the **well-known limitations of any time series model**, and there are ways to examine those challenges. So again, we first have to start with an appropriate theoretical model. Of course, **you could put two variables that trend together in a model and there's no sensible relationship, and clearly that would be spurious**.[229]

- Q. And why is nonstationarity an issue with time series models?

  A. **If you have this problem, which again, we do not, then you can get spurious results.**[230]

- Q. Do you know if the MME prescriptions in your model are stationary?

  A. As I sit here, no.

  Q. Do you know if the stock of detailing variable is stationary?

  A. Again, as I sit here, no.

  Q. And would the presence of nonstationarity lead you to overstate the impact of promotion in your direct model?

  A. Well, again, if the – **if there was a unit root problem, then it could overstate the results, yes**.[231]

Professor Rosenthal incorrectly asserts that her model does not suffer from this issue. I used the standard test for stationarity, the same test that Professor Rosenthal purportedly ran, and I conclude that neither MME prescriptions nor detailing stock are stationary.[232] As Professor Rosenthal herself described the "well-known limitations of any time series model," a regression of two non-stationary variables can produce results that are overstated at best and completely spurious at worst.

(117) Non-stationary time series are common in econometrics, so fortunately there are established corrections.[233] In particular, I implemented two standard corrections in Professor Rosenthal's preferred model to reduce the problematic nonstationarity: (1) a "first-differences" model that predicts monthly changes in prescription MMEs from monthly changes in detailing stock, and (2) a "log-log" model that predicts percentage changes in MMEs from percentage changes in detailing

[229] Rosenthal May 4 Dep. at 134:10–25 (emphasis added).

[230] Rosenthal May 4 Dep. at 138:16–20 (emphasis added).

[231] Rosenthal May 4 Dep. at 139:13–24 (emphasis added).

[232] Specifically, I ran a Dickey-Fuller test. Professor Rosenthal claims to have relied upon the same test: "we looked at a Dickey-Fuller test, which is basically testing for unit roots. I'm thinking about the simple explanation goes to what you said before about two slow-moving trends and whether there might be spurious correlation, and we found that those concerns were not warranted based on the Dickey-Fuller results." Rosenthal May 4 Dep. at 137:15–23.

[233] R. Carter Hill and William E. Griffiths, Principles of Econometrics, Fourth ed. (Danvers, MA: John Wiley & Sons, 2011), 483.

stock. I otherwise maintained Professor Rosenthal's flawed framework. The relationship between detailing stock and MMEs is not statistically significant in the first-differences model and is statistically significant but greatly reduced in the log-log model, such that detailing stock explains very little, if any, of the variation in opioid MMEs over time. The small but statistically significant effect of detailing stock in the log-log model suggests that only 3% of total MMEs are associated with Defendant detailing. Even this estimate is likely an overstatement of the true effect of promotion given the numerous other technical flaws and omitted variables in Professor Rosenthal's model, as detailed below. The first-differences and log-log results confirm that Professor Rosenthal's nearly perfect purported relationship between detailing and MMEs is a spurious result produced by her violation of basic economic principles.

Figure 29: Summary of first differences model

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	40,732,347		-30,994,138		-84,729,648	
b	First difference of Stock of Promotion	16,753	**				
b1	First difference of Stock of Promotion*Regime Dummy until Oct2001			1,862		3,041	
b2	First difference of Stock of Promotion*Dummy from Oct2001			3,581		6,514	
b3	First difference of Stock of Promotion*Dummy Trend from Jan2010			-82		-1	
evt1	Consensus Statement From AAPM/APS 01/1998					8,266,239	
evt2	Federation of State Medical Boards Guidelines 01/1999					10,314,321	
evt3	JCAHO pain standards releases 01/2001					-138,574,178	
evt4	OxyContin Reformulation 08/2010					-308,152,265	
evt5	Hydrocodone Rescheduling 10/2014					6,614,512	
main0	First difference of Fisher Ideal Price Index	-1,170,154,552		-1,143,252,841		-1,063,379,393	
x	Depreciation constant	1.4775	***	-0.0012		-0.0027	
RSquare		0.0294		0.0179		0.0224	
AdjRSq		0.0197		0.0014		-0.0110	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 30: Summary of Log-Log sensitivity

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	20.1160	***	17.9443	***	23.5406	***
b	Log of Stock of Promotion	0.2017	***				
b1	Log of Stock of Promotion*Regime Dummy until Mar2002			0.2453	***	-0.3055	***
b2	Log of Stock of Promotion*Dummy from Mar2002			0.2551	***	-0.2712	***
b3	Log of Stock of Promotion*Dummy Trend from Aug2010			-0.0005625	***	-0.0016565	***
evt1	Consensus Statement From AAPM/APS 01/1998					0.5730	***
evt2	Federation of State Medical Boards Guidelines 01/1999					0.4475	***
evt3	JCAHO pain standards releases 01/2001					0.2281	***
evt4	OxyContin Reformulation 08/2010					0.5102	***
evt5	Hydrocodone Rescheduling 10/2014					-0.0657	
main0	Fisher Ideal Price Index	-1.8475	***	-0.2844	***	1.1301	***
x	Depreciation constant	-0.0911	***	-0.0534	***	0.2496	***
RSquare		0.9435		0.9850		0.9672	
AdjRSq		0.9428		0.9846		0.9657	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 31: Overall percentage impact of Defendant promotion on MMEs, Log-Log model

Year	Model A	Model B	Model C
1995	0.4%	0.9%	-11.9%
1996	0.8%	1.9%	-16.3%
1997	0.9%	2.4%	-13.0%
1998	0.9%	2.6%	-14.8%
1999	0.9%	2.8%	-22.3%
2000	1.0%	3.0%	-29.9%
2001	1.0%	3.1%	-33.7%
2002	1.0%	3.2%	-35.4%
2003	1.0%	3.3%	-32.6%
2004	1.0%	3.3%	-25.9%
2005	1.0%	3.3%	-26.3%
2006	1.0%	3.3%	-27.8%
2007	1.0%	3.3%	-24.4%
2008	1.0%	3.3%	-20.2%
2009	1.0%	3.3%	-20.3%
2010	1.0%	3.3%	-22.0%
2011	1.0%	3.2%	-18.1%
2012	1.0%	3.1%	-19.8%
2013	1.0%	3.1%	-34.5%
2014	1.0%	3.0%	-40.0%
2015	1.0%	2.9%	-34.1%
2016	1.0%	2.8%	-22.4%
2017	1.0%	2.7%	-20.3%
2018	1.0%	2.6%	-18.7%
TOTAL	**0.9%**	**2.9%**	**-24.5%**

Source: Rosenthal backup data.

(118) In addition to her violation of the nonstationarity assumption, Professor Rosenthal ignores the conclusion of the economics and marketing literatures that promotional activities and sales are simultaneously determined, or endogenous. While promotion may cause an increase in sales, it is also possible that sales drive promotion. There are two possible channels for this causality. First, manufacturers target high prescribers for detailing. That is, they use observed sales to guide their promotional activities, and detailing follows sales; this also makes the effect of promotion very difficult to disentangle from physician learning-by-doing or experience. Second, manufacturers may promote successful products more intensively. Consequently, promotion cannot be considered an independent variable in the regression, and failure to address its endogeneity produces biased estimates. In a meta-analysis of 58 studies, Kremer et al. (2008) conclude this failure biases the estimated elasticity of advertising on sales by about 0.21.[234] It is therefore highly likely that Professor Rosenthal's estimate overstates the causal effect of detailing on prescription-based MMEs. This is particularly the case for Allergan, which as I describe throughout this report, targeted prescribers for

[234] Sara T.M. Kremer, Tammo H.A. Bijmolt, Peter S.H. Leefland, Jaap E. Wieringa, "Generalizations on the effectiveness of pharmaceutical promotional expenditures," *International Journal of Research in Marketing* 25, no. 4 (2008), 244.

Kadian detailing with the objective of either maintaining Kadian prescribing or substituting for other products. In addition, the very micro-level evidence on prescribers detailed in Cuyahoga and Summit counties described earlier shows that Allergan detailing did not increase Kadian prescriptions for 39 of the 41 physicians, consistent with a very small elasticity of sales with respect to detailing at the physician level.

(119) Professor Rosenthal acknowledges the potential for bias due to selective detailing in her report: "While these latter two studies demonstrate the magnitude of industry 'transfers of value' to physicians related to opioid prescribing, they do not attempt to identify a causal effect of marketing on sales. As the authors acknowledge, the contemporaneous association between payments and prescriptions may be caused by industry targeting of payments to high prescribers."[235] The literature similarly concludes that ignoring the selection of physicians for detailing will overstate the effect of promotion. For example, Datta and Dave (2016) state that their estimated effect of promotion after inclusion of prescriber fixed effects to account for selection "is substantially smaller than those in the literature based on aggregate information, suggesting that most of the observed relationship between physician-directed promotion and drug sales is driven by selection bias."[236] They also note that their estimate "is substantially lower than that reported in prior studies that do not account for endogeneity, suggesting that most of the observed association between detailing and drug sales reflects unobserved selection."[237]

(120) Professor Rosenthal asserts that her use of an aggregate national model avoids the overwhelming consensus in the literature that sales, promotion, and price are endogenous:

> It simply doesn't exist in my data because I'm not looking at physician-level data. I cannot mistake the fact that Doctor A has high prescriptions compared to Doctor B, not because she's been detailed before, but she's been detailed before because she has high prescriptions. Because I'm only looking at the aggregate. So the only kind of endogeneity there, it can't be related to targeting. It has to be related to something else.
>
> In other instances people have looked at endogeneity when it comes to a specific product. They said, well, you know, we knew that this product was going to be a blockbuster so we put our detailing on product A versus product B, and so that's the

[235] Rosenthal Rep. ¶ 42.

[236] Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," Health Economics 26 no. 4 (2016), 460.

[237] Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," Health Economics 26 no. 4 (2016), 465.

> nature of the endogeneity. But again, I don't have that here because I'm aggregating across products.[238]

Although she does not rely on cross-sectional data, for which the selection of physicians would be a major source of endogeneity bias, it is nevertheless still true that sales, promotion and price are simultaneously determined at the aggregate level. Many econometrics textbooks use the endogeneity of aggregate supply and demand to illustrate the difficulty of identifying how a change in price affects demand. Aggregation does not eliminate all sources of endogeneity.

(121) The academic papers using the closest approach to Professor Rosenthal[239] address the endogeneity of promotion. Her failure to do so is therefore surprising. Indeed, Professor Rosenthal herself has previously acknowledged in publications and expert reports that an instrumental variables ("IV") approach is required to address endogeneity.

- Zyprexa: "In addition, the estimation deals with two important issues: serial correlation in the error terms and the endogeneity of price and promotion. Serial correlation in the error terms required the use of time-series methods to produce reliable estimates. The endogeneity of price and promotion was handled using the standard instrumental variables approach."[240]
- Neurontin: "The model also accounts for the fact that price and promotion are codetermined with the quantity of Neurontin. The endogeneity of price and promotion was handled using the standard instrumental variables approach."[241]
- Rosenthal (2003): "We account for the possibility that spending on DTCA and physician promotion and product sales are jointly determined by estimating instrumental variables (IV) models where all three variables are assumed to be endogenous."[242]
- One way to assess the presence of endogeneity is to test for reverse causation. Reverse causation is generally characterized as a situation in which the dependent variable is causing changes in the independent variable rather than being caused by the independent variable, which is the opposite causal direction assumed by a regression analysis. In the context of Professor Rosenthal's flawed direct models, the existence of a statistically significant relationship between next month's detailing and the current month's prescription MMEs reflects potential reverse causation. Figure

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238 Rosenthal May 4 Dep. at 333:5–24.

239 *See* Ernst R. Berndt, Linda Bui et al., "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *American Economic Review* 85, no. 2 (1995), 100–105.

240 Exhibit E, Declaration of Meredith Rosenthal, *Hood v. Eli Lilly & Co*, No. 1:07-cv-00645-JBW-RLM, Dkt. 208-4, at 4772 (E.D.N.Y Oct. 9, 2009) ¶ 36–38.

241 Estimate Of Units Paid For By Neurontin Endpayers That Resulted From Alleged Fraudulent Marketing By Defendants: Declaration of Meredith Rosenthal, *In re Neurontin Marketing, Sales Practices, and Products Liability Litigation*, MDL Docket No. 1629, Master File No. 04-10981, (D.Ma. September 14, 2006)

242 Meredith B. Rosenthal et al., "Demand Effects of Recent Changes in Prescription Drug Promotion," in Frontiers in Health Policy Research, Vol. 6, eds. David M. Cutler and Alan M. Garber, (Cambridge, MA: The MIT Press, 2003), 15.

32 summarizes the results of this test. The relationship between next month's detail contacts and current MMEs is positive and statistically significant in all three of Professor Rosenthal's direct model specifications. This result suggests that opioid MMEs explaining the variation in manufacturer detailing is just as plausible as Professor Rosenthal's finding that manufacturer detailing explains the variation in opioid MMEs.

Figure 32: Summary of promotion lead sensitivity

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	3,079,551,769	**	2,174,294,724	***	2,303,890,980	***
b	Stock of Promotion (All promotion)	2,802	***				
b1	Stock of Promotion (All promotion)*Regime Dummy until Mar2002			930	***	932	***
b2	Stock of Promotion (All promotion)*Dummy from Mar2002			1,127	***	1,124	***
b3	Stock of Promotion (All promotion)*Dummy Trend from Aug2010			-8	***	-8	***
d	Lead of contacts (contacts t+1)	70,684	***	7,172	**	9,348	**
evt1	Consensus Statement From AAPM/APS 01/1998					-327,748,550	*
evt2	Federation of State Medical Boards Guidelines 01/1999					341,908,494	*
evt3	JCAHO pain standards releases 01/2001					-49,480,128	
evt4	OxyContin Reformulation 08/2010					-109,120,147	
evt5	Hydrocodone Rescheduling 10/2014					595,914,013	***
main0	Fisher Ideal Price Index	-7,510,229,871	***	-1,929,961,740	***	-2,106,026,676	***
x	Depreciation constant	0.0000		-0.0066	***	-0.0067	***
RSquare		0.8998		0.9938		0.9941	
AdjRSq		0.8984		0.9937		0.9939	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

(122) Professor Rosenthal elects to use aggregate data, which is the result of summing over all drugs, manufacturers, physicians, and counties in each month to arrive at a dependent variable for all MMEs nationally, regressed on all detailing contacts nationally. Underlying her regression specification, though not explicitly specified in her report, is a microeconomic model of how physicians (acting as agents for their patients) write prescriptions in response to detailing visits. Moving from "micro" data – that is, observations at the drug-physician-state level – to the "macro" level introduces the possibility of aggregation bias. That is, relationships estimated from aggregate data may be very different from the "true" relationship that exists at the micro level. This is particularly true if there is substantial heterogeneity at the micro level.[243]

[243] As Clark and Avery (1976) note, "The consequences of using potentially biased estimates of the correlation and

(123) As discussed in Section II.A, physicians are known to be heterogeneous along many dimensions, including their sensitivity to pharmaceutical promotion. The specific products are also heterogeneous: they have different chemical properties, they are not equally prone to abuse, they do not have equal positions on formularies, etc. Finally, counties are heterogeneous, with different observable and unobservable economic conditions that influence demand for opioids. Thus, while Professor Rosenthal maintains that an aggregate model is appropriate for her assignment, she ignores the potential bias introduced by aggregating over very heterogeneous units. In addition, the estimates she produces are not useful for inferring county-level outcomes, as Professors Cutler and McGuire do, because applying results from an aggregate model to a smaller unit is a commission of the "ecological fallacy."

(124) Finally, setting aside the nonstationarity and endogeneity issues described above, Professor Rosenthal's conclusions are sensitive to principled changes to her data inputs and model specifications.[244] Testing the sensitivity of several of these changes produces implausible results that demonstrate the fragility of her approach. For example:

- Adjusting Professor Rosenthal's direct model decay rate to values observed in literature (i.e., 0%, 5%, 20%, and 40%) substantially reduces the estimated percentage impact of Defendant detailing. I list the results of these sensitivities in Appendix D.
- I explain in Section VI.B that adjusting Professor Rosenthal's price index to use MMEs (as she prefers elsewhere in her model) produces a price index that declines during most of the relevant time period, in contrast to her price index based on extended units that increases throughout the relevant time period. Running her preferred model using the corrected price index results in a nonsensical positive effect of price, which implies that that higher average prices are associated with more prescription MMEs. This result is inconsistent with both economic theory and common sense and is indicative of an underlying problem with her model.

regression coefficients as substitutes for the 'true' microlevel estimates are most serious in terms of the causal inferences to be drawn from statistical analyses." W.A.V. Clark and Karen L. Avery (1976), "The Effects of Data Aggregation in Statistical Analysis", Geographic Analysis 8(4), 428–438;

In a survey of approaches to addressing heterogeneity in aggregate data, Blundell and Stoker (2007) state that "aggregation problems are likely to lead to serious bias" Richard Blundell and Thomas M. Stoker (2007), "Models of Aggregate Economic Relationships that Account for Heterogeneity," Handbook of Econometrics Vol. 6A, Chapter 68, pp. 4609–4666;

Aggregation bias has been demonstrated in many other contexts, including crime and hospital costs. Todd L. Cherry and John A. List (2002), "Aggregation bias in the economic model of crime," Economics Letters 75, 81–86; Feigenbaum et al., "Medicare's Prospective Payment System: The Victim of Aggregation Bias?" *Review of Economics and Statistics* 74, no. 1 (1992), 185-191.

[244] It is standard practice for economists to confirm that their results are not sensitive to these types of changes. For example, Datta and Dave (2016) confirm that their "[r]esults are not materially affected under alternate measures of the decay rate ranging from 0 to 0.4." Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," Health Economics 26 no. 4 (2016), fn 23.

- I explain previously in this section that the use of a log-log specification nearly eliminates the estimated impact of manufacturer detailing on opioid MMEs. In addition to reducing concerns about nonstationarity, log transformations of sales and detailing are standard in the economics and marketing literature, particularly when using aggregate data. The linear specification used by Professor Rosenthal assumes that a one-unit increase in the stock of detailing is associated with a beta increase in MMEs, while a log specification assumes that a 1% increase in the stock of detailing is associated with a beta% increase in MMEs. In other words, in the linear model, adding detailing in the very beginning of the opioid market has the same marginal impact on contemporaneous MMEs as adding detailing in 2008. However, one additional detail at the beginning represents a much larger percentage increase in the stock of details than one additional detail in 2008. Economists prefer the log specification because it estimates the marginal impact of one percent change in detailing, rather than a one-unit change.

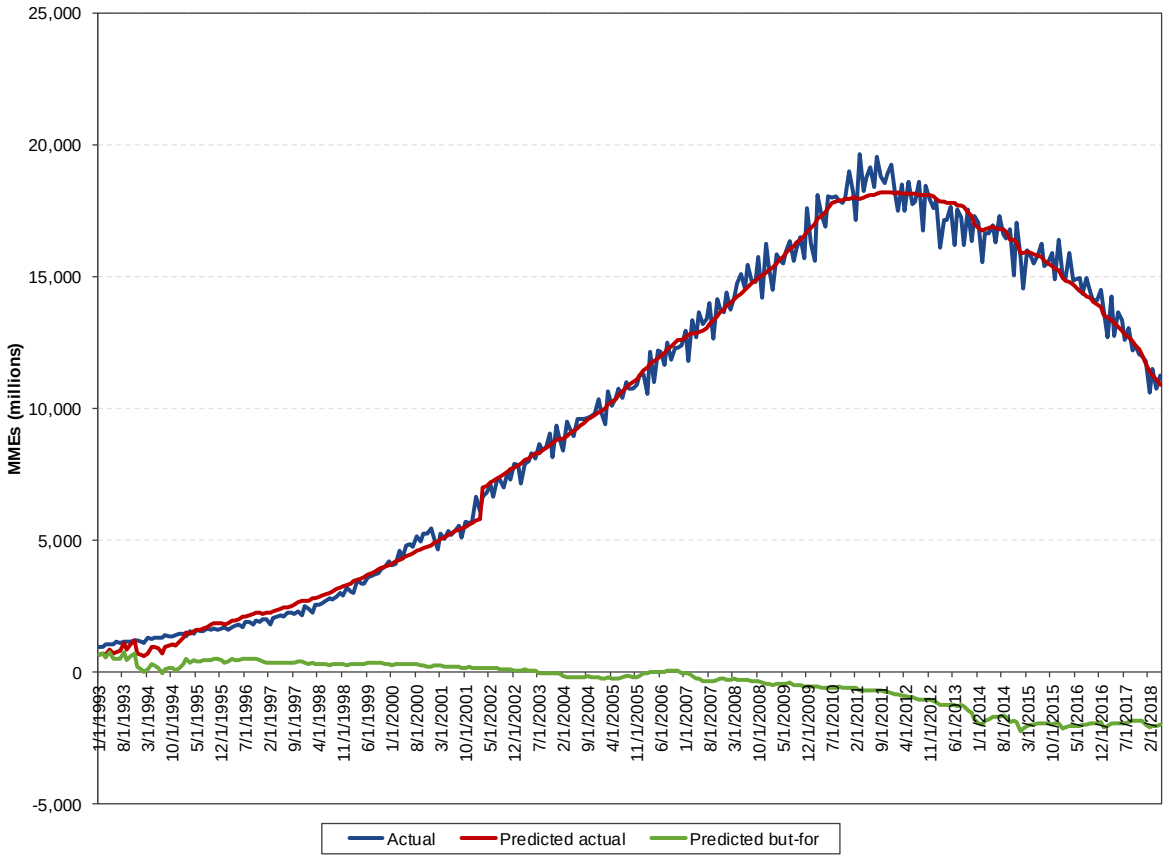
VI.B. Professor Rosenthal's direct causation model is a goal-seeking exercise that assumes its conclusion

(125) Professor Rosenthal couches her model in the language of "standard econometric technique[s]" and describes the general approach as "in line with the published literature," but her specific modelling choices lack theoretical justification and are inconsistent with published literature. Rather, her choices appear to be designed to maximize the estimated relationship between promotion and prescription-based MMEs, at the expense of economic theory and common sense. As I describe further below, by allowing the data to determine the depreciation rate and turning points with arbitrary interactions, she has created a model flexible enough to fit any pattern of MMEs, but one that is incapable of accurately quantifying correlation or causation.

(126) The goal-seeking nature of Professor Rosenthal's model is plainly evident in her model results. Though Professor Rosenthal describes a large number of factors that influence physician prescribing, her model purports to explain 99% of prescribing solely on the basis of manufacturer detailing and price.[245] Indeed, as shown in Figure 33 below, Professor Rosenthal's model attributes so much explanatory power to manufacturer promotion that it predicts prescribing would be *negative* as early as 2003 in the absence of promotion. In the remainder of this section, I provide examples of specific atheoretical and economically inappropriate modeling choices Professor Rosenthal makes in her effort to maximize fit.

[245] Rosenthal Rep. ¶ 72.

Figure 33: Professor Rosenthal's "model B" predicted MMEs in the absence of manufacturer promotion



Source: Rosenthal backup data

(127) One of Professor Rosenthal's results, which she acknowledges is "at odds with the usual marketing literature," is an estimate of a negative depreciation rate:[246]

> Q. As you sit here right now, do you know of any literature, whether related to nonaddictive or addictive products, that has a negative depreciation rate?
>
> A. I cannot point to any other study, no.[247]

Professor Rosenthal estimates a model that relates the stock of promotion across all manufacturers to total opioid prescription-based MMEs contemporaneously. The stock of detailing reflects flows of promotional efforts in each period added to all prior detailing efforts, which is allowed to depreciate (or appreciate) over time. She estimates this depreciation rate directly in her model.

[246] Rosenthal Rep. ¶ 72.

[247] Rosenthal May 4 Dep. at 259:25–260:6.

(128) In practice, it is difficult to estimate the independent effects of the stock of detailing and the depreciation rate. As Datta and Dave (2016) point out:

> An unbiased estimate of the depreciation rate would require a detailed structural modeling of promotion and prescription behaviors; without which, it would be difficult to disentangle the coefficient of the detailing stock from the depreciation rate (Iizuka and Jin, 2005). Prior research on consumer behavior suggests that advertising effects fully depreciate within 6 months to a year, consistent with decay rates of 0.1–0.2 (Bagwell, 2007), which have also been found to apply to pharmaceutical advertising (Iizuka and Jin, 2005; Ling et al., 2002).[248]

While Professor Rosenthal's model is superficially similar to those used in other economics papers, these papers (as well as Professor Rosenthal's past work and model A in this report) estimated positive depreciation rates, which implies that the effects of promotion decline over time.[249] These estimates are in stark contrast to the negative depreciation rate estimated by Professor Rosenthal in her preferred model in this case. Her negative depreciation rate instead implies that the effects of promotion actually grow stronger over time.

(129) The effect of this estimate can be seen in Figure 34. The blue line represents actual details, which exhibit wide variation through time. The green line shows increasing promotional stock assuming promotion accumulates with no depreciation (i.e., the effect persists indefinitely), and the brown line shows that under a more typical positive depreciation rate of 0.01, the stock of detailing would be largely flat. In contrast, the red line shows the negative depreciation rate estimated in Professor Rosenthal's preferred model—it transforms the noisy blue pattern, which bears no resemblance to the opioid MME growth pattern into an exponential growth curve that closely tracks the actual growth pattern of opioid MMEs, allowing Professor Rosenthal to find a stronger relationship than actually exists.

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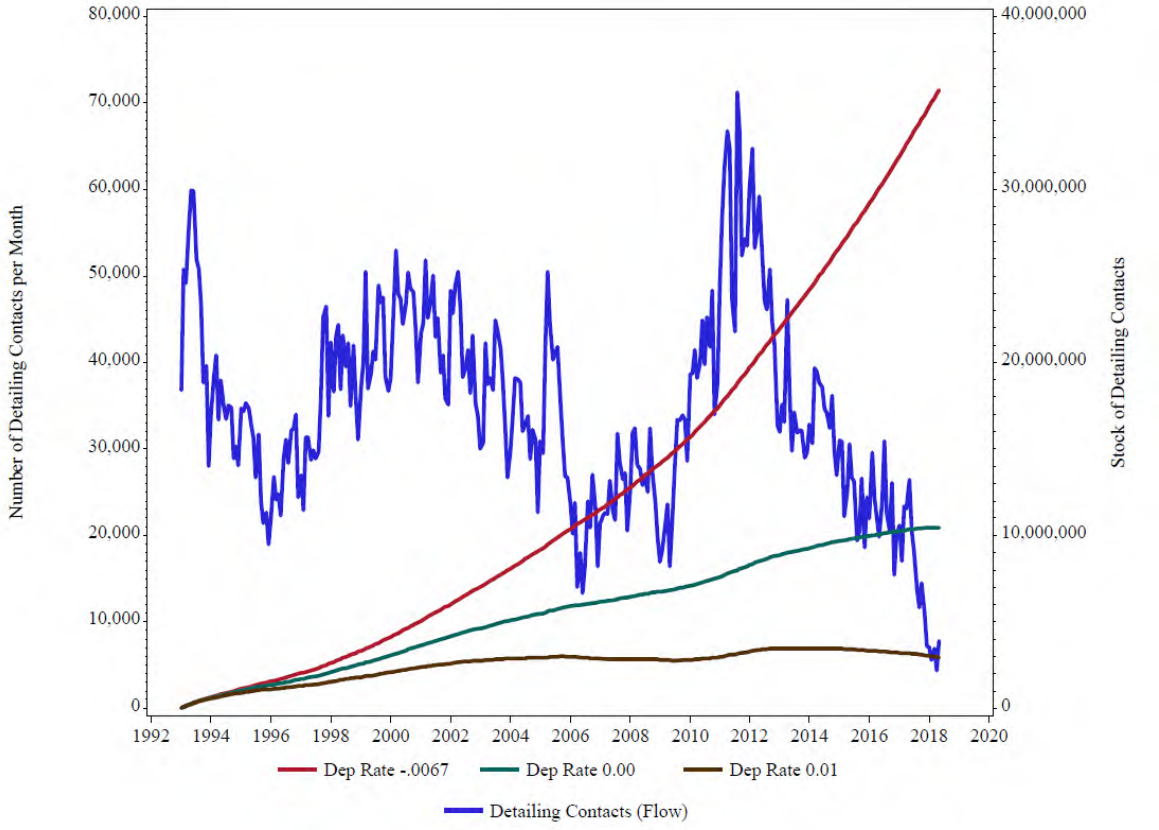
[248] Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," Health Economics 26 no. 4 (2016), fn 23.

[249] *See* Ernst R. Berndt, Linda Bui et al., "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," American Economic Review 85, no. 2 (1995), 100–105.;

See Davina C. Ling, Ernst R. Berndt, and Margaret K. Kyle, "Deregulating Direct-to-Consumer Marketing of Prescription Drugs: Effects on Prescription and Over-the-Counter Product Sales," Journal of Law and Economics 45 no. 2 (2002), 691–723.;

See also Meredith B. Rosenthal, Ernst R. Berndt, Julie M. Donohue, "Demand Effects of Recent Changes in Prescription Drug Promotion," in Frontiers in Health Policy Research, Vol. 6, eds. David M. Cutler and Alan M. Garber, 1–26 (Cambridge, MA: The MIT Press, 2003).

Figure 34: Professor Rosenthal's detailing stock under three depreciation rates (Rosenthal Figure 4)



Source: Rosenthal Rep. Figure 4.

(130) Professor Rosenthal's negative depreciation is inconsistent with industry patterns and economic literature that suggest marketing efforts fall as patent expiration approaches (a pattern observed with Kadian), and the total number of prescriptions drops, on average, once marketing stops.[250] Nathalie Leitch, Actavis Director of Specialty Rx, explains this concept with respect to Kadian as it was nearing patient expiration:

> Given our short runway with the product, we had a very limited time in the market, we believed, until the patents expired. We decided that taking a very modest approach to—to building a sales team and putting a commercial effort behind the product was—was the right way to go. It—it would stem the decay or stem the—the loss in sales of the product.[251]

[250] *See* Peter J. Huckfeldt and Christopher R. Knittel, "Pharmaceutical Use Following Generic Entry: Paying Less and Buying Less," NBER Working Paper #17046 (2011), 1–48.

[251] Leitch Dep. at 40:9–40:16.

Though Professor Rosenthal acknowledges her negative depreciation rate is inconsistent with economic theory and the empirical literature, both she and Professor Cutler claim that a negative depreciation rate is not surprising because of the addictive nature of opioids, and reference economic theories of rational addiction.[252] However, these theories apply to an individual's *consumption* of a good, not a prescriber's exposure to marketing. Studies of other addictive products, such as cigarettes, have found positive depreciation rates.[253] In addition, empirical tests of such models—particularly when using aggregate data and allowing depreciation rates to be chosen by the data—can produce dubious results, indicating that products such as milk and eggs are "addictive."[254] While a physician may write a sequence of prescriptions for a patient whose tolerance increases or who becomes addicted, physicians also write a sequence of prescriptions for patients with chronic diseases (such as ulcers), and the stock of detailing in such studies has not been estimated to appreciate over time. In addition, physicians who observe significant numbers of patients developing an addiction to prescription opioids would presumably update their assessment of their risks, and start fewer new patients on opioid therapy. The addictive nature of opioids is therefore not a sound justification for a negative appreciation rate for the stock of promotion.

(131) Professor Rosenthal also incorrectly describes her direct model's approach to her three time periods. Specifically, Professor Rosenthal writes:

> I model the effects of detailing on the number of MMEs sold at retail using a "piecewise" model, where the coefficient on the stock of detailing is estimated separately during each of the three eras. Not only does this approach correspond to observed changes in prescribing attitudes and guidelines for prescription opioids but also it tracks the patterns of the sales data presented in Figure 2.[255]

(132) However, Professor Rosenthal's model does not estimate the coefficient on the stock of detailing "separately during each of the three eras." Her model measures stock separately in the first and second periods as described, measuring a constant effect for promotional stock in each of the two time periods. During the third period, however, she allows the effect of the stock in the second period to persist, such that both second and third period stocks are allowed to explain opioid MME variation from August 2010 through 2018. In addition, she includes an interaction between the third period and a time trend such that the measured negative effect in the third period grows stronger during each month, above and beyond the 8% annual appreciation. This is not a standard "piecewise" model,

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[252] Rosenthal Rep. ¶ 72; Cutler April 26 Dep. at 177–179; Rosenthal May 4 Dep. at 259:25–260:4.

[253] *See also* Shi Qi, "the Impact of Advertising Regulation on Industry: The Cigarette Advertising Ban of 1971," *The RAND Journal of Economics* 44, no. 2 (2013), 215–248;

Mark J. Roberts and Larry Samuelson, "An Empirical Analysis of Dynamic, Nonprice Competition in an Oligopolistic Industry," *The RAND Journal of Economics* 19, no. 2 (1988), 200–220.

[254] M. Christopher Auld and Paul Grootendorst, "An empirical analysis of milk addiction," *Journal of Health Economics* 23, no. 6 (2004), 1130.

[255] Rosenthal Rep. ¶ 68

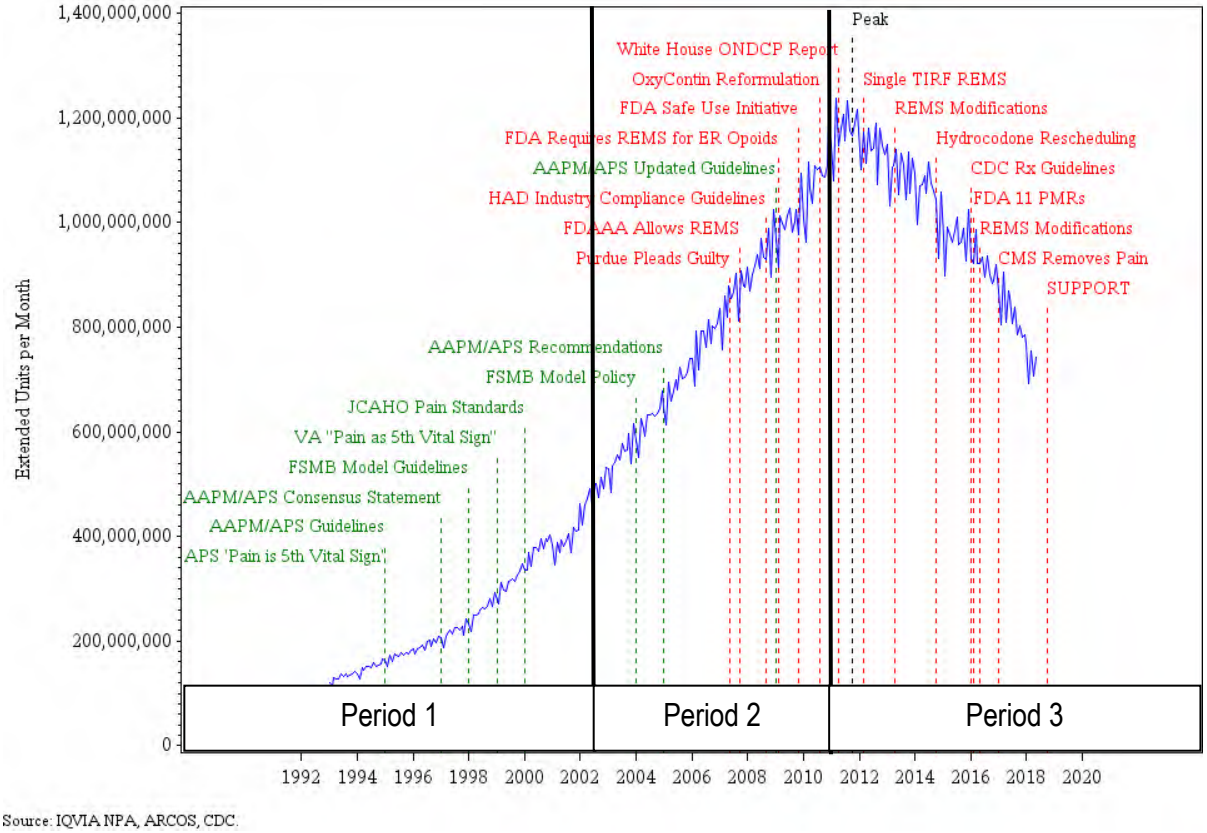
which would allow for a different constant slope (or effect of the stock of promotion) in each period, but a flexible model that is constructed to perfectly track the declining third-period trend in MMEs without economic justification. The introduction of a time trend in the third period is especially puzzling, as Professor Rosenthal elsewhere criticizes such an approach by stating that "the introduction of a time trend is not an appropriate explanatory variable when one is trying to explain the cause of a trend as opposed to trying to exclude the impact of the trend."[256]

(133) The choice of turning points similarly lacks any economic justification. Normally, the decision to estimate different effects during different time periods is motivated by changes in the economic environment that are otherwise not controlled for, such as a shift in the regulatory or legal environment. No specific regulatory or promotional event is cited or included in her timeline for March 2002 and August 2010, her chosen breakpoints. Indeed, though she identifies 23 distinct "key events" that "helped promote expanded opioid prescribing (in green), and subsequent public health and regulatory events (in red)" those events do not correspond to the time periods she uses in her model.[257] As shown in Figure 35 below, Professor Rosenthal's first period during which promotion has a lesser effect contains the majority of the events that she describes as "help[ing] promote expanded opioid prescribing. Her second period during which she "allow[s] for an additive shift in promotional effectiveness" includes a number of the "public health and regulatory events" she describes.

[256] Rosenthal Rep. Appendix D6.

[257] Rosenthal Rep. ¶ 57, Figure 5.

Figure 35: Professor Rosenthal's "Timeline of Key Events" and the three periods of her model



Source: IQVIA NPA, ARCOS, CDC

(134) In fact, Professor Rosenthal develops no *a priori* hypotheses for why/when these turning points exist. Instead, she estimates her model 1,176 times, each with a different combination of turning points, and selects the specification that has the highest Wald statistic. This atheoretical approach to modelling is generally discouraged in economics, and it invalidates the statistical assumptions required for inference. A prominent economist and statistician at UCLA, Edward Leamer, describes the issue as follows:

> The econometric art as it is practiced at the computer terminal involves fitting many, if not thousands, of statistical models. One or several that the researcher finds pleasing are selected for reporting purposes…all the concepts of traditional theory…utterly lose their meaning by the time an applied researcher pulls from the bramble of computer output the one thorn of a model he likes best, the one he chooses to portray as a rose.[258]

[258] Edward E. Leamer, "Let's Take the Con out of Econometrics," The American Economic Review 73, no. 1 (1983), 36–37.

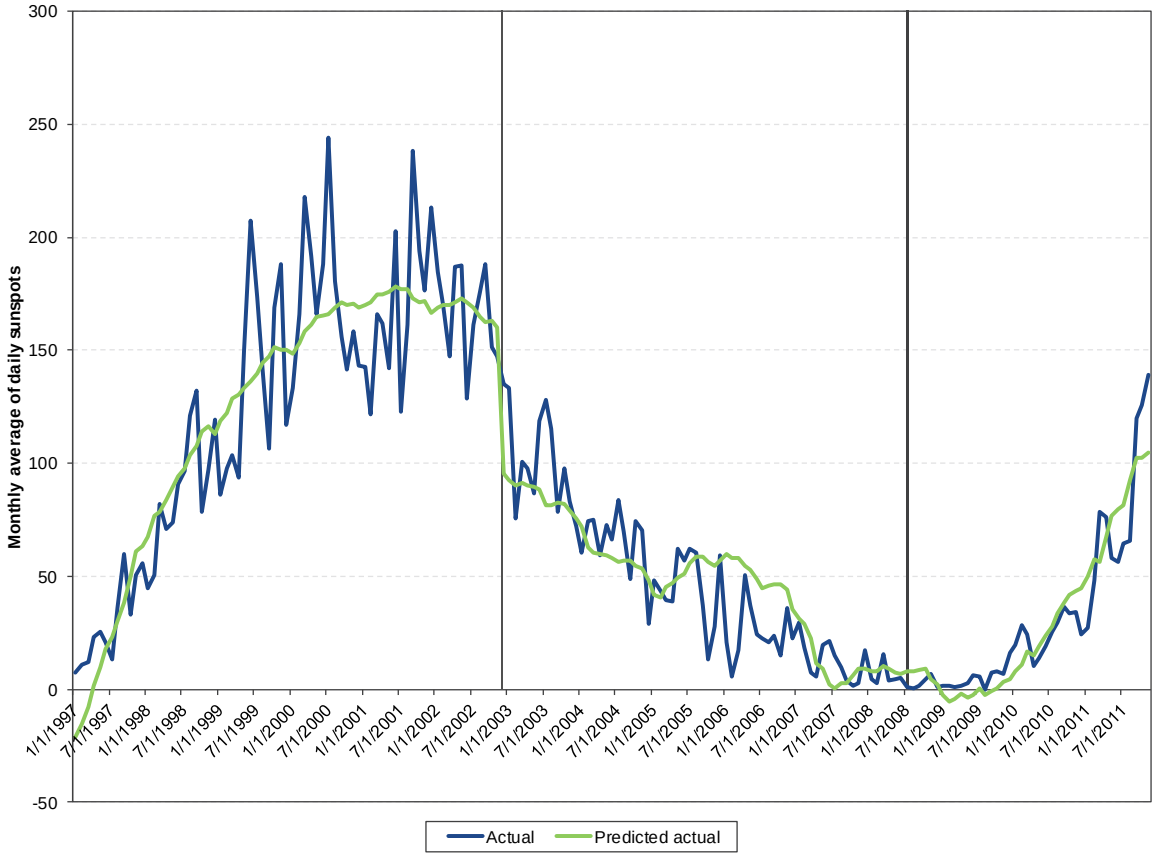
(135) To illustrate the flaws in this approach, I run an alternate version of Professor Rosenthal's model in which I replicate her methodology, but rather than predicting the number of MMEs sold, I use her approach to predict an unrelated variable. For this analysis, I use data from NASA on the monthly average of daily sunspots from January 1997 through November 2011. Similar to Professor Rosenthal, I allow the model to select two turning points based on the maximum Wald statistic and allow the model to estimate the depreciation rate. For Model C, I use the same events as Professor Rosenthal, with the exception of the Hydrocodone Rescheduling date because this falls outside of the range of sunspot data. Figure 36 below summarizes the coefficients on the variables for Model B and Model C, and Figure 37 below illustrates the actual and predicted values for Model B. Despite the fact that manufacturer detailing and opioid prices definitively do not cause sunspots, the coefficients on the three detailing stock variables and the price index are statistically significant. Furthermore, the model fits the sunspot data well, with an adjusted R-squared of 0.88, suggesting that detailing and price explain 88% of the variation in sunspots.

Figure 36: Impact of detailing on monthly average of daily sunspots

Parameter	Label	Model B		Model C	
		Estimate	Sig.	Estimate	Sig.
a	Constant	154	***	87	**
b1	Stock of Promotion (All promotion)*Regime Dummy until Dec2002	0.0003	***	0.0004	***
b2	Stock of Promotion (All promotion)*Dummy from Dec2002	0.0002	***	0.0003	***
b3	Stock of Promotion (All promotion)*Dummy Trend from Jul2008	0.000002	***	0.000002	***
evt1	Consensus Statement From AAPM/APS 01/1998			-30	**
evt2	Federation of State Medical Boards Guidelines 01/1999			-6	
evt3	JCAHO pain standards releases 01/2001			-26	**
evt4	OxyContin Reformulation 08/2010			-21	
main0	Fisher Ideal Price Index	-172	***	-107	***
x	Depreciation constant	0.0648	***	0.0545	***
RSquare		0.8787		0.8883	
AdjRSq		0.8752		0.8823	

Source: Rosenthal backup data; NASA sunspot data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 37: Actual vs. predicted monthly average of daily sunspots



Source: Rosenthal backup data; NASA sunspot data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

(136) Professor Rosenthal's model is thus a goal-seeking exercise to maximize the relationship between promotion and MMEs. Allowing the data to determine the depreciation rate and turning points with arbitrary interactions makes the model flexible enough to fit almost any pattern, from opioid prescription MMEs to a completely unrelated time series. This approach yields results that are contrary to economic theory and to common sense, and renders her model incapable of demonstrating or quantifying a causal relationship between promotion and MMEs.

VI.C. Professor Rosenthal's direct and indirect causation models ignore myriad other factors that influence prescribing, including many identified by other Plaintiff experts

(137) Professor Rosenthal's models purport to measure the percentage of MMEs "caused by unlawful promotion" using an "econometrically sound method."[259] But in her preferred direct model, Professor

[259] Rosenthal Rep. ¶ 11, 74.

Rosenthal tests only detailing and price, assuming that no other factors—including those she herself identifies—have any effect on prescribing. This issue is not limited to Professor Rosenthal's preferred model, however.[260] In this section, I identify several potentially confounding factors that Professor Rosenthal fails to include in any of her models. In failing to consider certain factors that might explain the variation in opioid MMEs, Professor Rosenthal ignores basic principles of econometrics and generates a model that is incapable of establishing causality.[261]

(138) As Professor. Daniel L. Rubinfeld explains (in the text cited by Professor Cutler to introduce his direct model):

> **An attempt should be made to identify additional known or hypothesized explanatory variables, some of which are measurable and may support alternative substantive hypotheses** that can be accounted for by the regression analysis.
>
> …
>
> **Failure to include a major explanatory variable** that is correlated with the variable of interest in a regression model **may cause an included variable to be credited with an effect that actually is caused by the excluded variable**. In general, omitted variables that are correlated with the dependent variable reduce the probative value of the regression analysis. The importance of omitting a relevant variable depends on the strength of the relationship between the omitted variable and the dependent variable and the strength of the correlation between the omitted variable and the explanatory variables of interest. Other things being equal, the greater the correlation between the omitted variable and the variable of interest, the greater the bias caused

[260] Professor Rosenthal's indirect model includes a handful of demographic variables, but ignores the other factors I describe that have known relationships to prescribing. Though I focus my discussion on these factors omission from her direct (preferred) model, these same factors would also cause her to overstate the effect of the alleged misconduct in her indirect model.

[261] Professor Rosenthal's prioritization of fit and predictive power over the inclusion of relevant explanatory variables is more appropriate for a predictive model than for a causal model.

"Three essential features of model choice are (1) choice of functional form, (2) choice of explanatory variables (regressors) to be included in the model, and (3) whether the multiple regression model assumptions MR1-MR6, listed in Chapter 5, hold….For choice of functional form and regressors, economic principles and logical reasoning play a prominent and vital role. We need to ask: What variables are likely to influence the dependent variable y?...Omission of a relevant variable (defined as one whose coefficient is nonzero) leads to an estimator that is biased. Naturally enough, this bias is known as omitted-variable bias…The possibilities of omitted variable bias or inflated variances from irrelevant variables mean that it is important to specify an appropriate set of explanatory variables." *See, e.g.,* R. Carter Hill and William E. Griffiths, *Principles of Econometrics*, Fourth ed. (Danvers, MA: John Wiley & Sons, 2011), 234–236.;

"Regression coefficients cannot be interpreted as causal if the relationship can be attributed to an alternate mechanism." Kenneth Frank, "Impact of a Confounding Variable on a Regression Coefficient," Sociological Methods & Research 29, no. 2 (2000), 147.

> by the omission. **As a result, the omission of an important variable may lead to inferences made from regression analyses that do not assist the trier of fact**.[262]

(139) Yet Professor Rosenthal does not even attempt to include such additional factors, despite identifying several in her report. In her industry background section, Professor Rosenthal lists numerous other factors that influence physician prescribing, including "patient preferences," "physicians…clinical skills, knowledge, and experience," "insurance coverage," "regulatory oversight" including "prescription drug labels," and many other types of promotion, none of which she attempts to measure.[263] The only variable other than contacts that Professor Rosenthal does choose to include in her preferred model—price—is the one she describes as having limited effect ("consumers and their physician-agents will be relatively insensitive to the **prices** of prescription drug therapies").[264]

(140) Professor Rosenthal also identifies 23 "key events identified by Plaintiffs" that helped promote (14) or regulate (9) opioid prescribing.[265] She attempts to incorporate only five of these events into her model, but concludes that they "barely improve[] upon the adjusted R-squared" so does not attempt to include others.[266] However, as I previously discussed, the small incremental effect is a direct result of Professor Rosenthal's flawed model construction. Because her model is designed to maximize the R-squared at the expense of interpretative value to the model, she attributes almost all MMEs to promotion and there is no room to add even those events that Plaintiffs themselves claim are key explanatory variables.

(141) Plaintiffs other experts also point to numerous factors other than detailing that influence prescribing:

- Professor Cutler identifies "many factors that go into…a physician's decision about prescriptions" including "belief about effectiveness," "prescribing standards of care," "restrictions in terms of prior authorization or cost," and "recommendations from senior colleagues or colleagues who are expert in a particular area."[267] Professor Cutler also identifies OxyContin reformulation, medical organization warnings, and federal and state enforcement as factors that decrease prescribing (Professor Rosenthal's model counterintuitively attributes this decrease to a new, *negative* effect of marketing that began in August 2010).[268]

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[262] Daniel L. Rubinfeld, "Reference Manual on Scientific Evidence: Third Edition," Federal Judicial Center; National Research Council (2011), 303–357. (emphasis added).

[263] Professor Rosenthal attempts to explain that her exclusion of other types of promotion is conservative, but as previously discussed in Section III, that exclusion is a bug, not a feature. Exclusion of other types of promotion (which Allergan did not conduct) causes her to attribute incorrectly the entire effect of that promotion to detailing (which Allergan did conduct). Rosenthal Rep. ¶¶ 12–22.

[264] Rosenthal Rep. ¶ 16.

[265] Rosenthal Rep. ¶ 57, Figure 5.

[266] Rosenthal Rep. ¶ 73.

[267] Cutler April 26 Dep. at 183:14–187:1.

[268] Cutler Rep. ¶ 52; Rosenthal Rep. ¶ 71.

- Professor Gruber identifies prescription drug monitoring programs ("PDMPs") and legal actions as factors that reduced prescribing, but also identifies "patient behavior, such as 'doctor shopping'" as well as "rogue clinics, or 'pill mills'" as factors that previously contributed to "excessive prescriptions."[269]
- Dr. Schondelmeyer identifies insurance coverage as a critical component in the supply chain, and specifically points to "the institution of the Medicare Part D prescription drug program in 2006" as an event that expanded prescription drug coverage.[270]
- Dr. Schondelmeyer also points to pharmacy benefit managers ("PBMs") as entities that "steer" patients using formularies, whose coverage decisions "are guided first by clinical considerations (i.e., safety and effectiveness) and then by economic considerations," as well as to generic substitution by pharmacists.[271]

(142) As I discuss in Section II.A, many of these factors are studied in the same body of economic literature that evaluates the impact of manufacturer promotion. For example, Epstein and Ketcham (2014, RAND) find that formulary status matters more than detailing (when physicians have access to formulary information through IT).[272] Other studies look at physician characteristics. Currie and Schnell (2018, American Journal of Health Economics) find that medical school experience influences opioid prescribing, and Janakiraman et al. (2008, Management Science) find that physicians are generally persistent in drug choice, and that those who are persistent are not responsive to detailing.[273] Though she had physician-level data available, Professor Rosenthal instead relies on an aggregate model that is incapable of evaluating any physician characteristics or clinical patterns that might influence prescribing decisions.

(143) The literature also identifies a number of demand-side factors, for example:

- Limitations by insurers on coverage of behavioral health therapy for chronic pain[274]
- Withdrawal from the market of non-opioid analgesics due to other health concerns (e.g., Vioxx)[275]

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269 Gruber Rep. ¶ 42.

270 Expert report of Dr. Stephen W. Schondelmeyer, March 25, 2019 [hereinafter "Schondelmeyer Rep."] ¶ 100.

271 Schondelmeyer Rep. ¶ 110-119.

272 Andrew J. Epstein and Jonathan D. Ketcham, "Information technology and agency in physicians' prescribing decisions," *RAND Journal of Economics* 45, no. 2 (2014), 422, 438–439.

273 Molly Schnell & Janet Currie, "Addressing the Opioid Epidemic: Is There a Role for Physician Education?," *American Journal of Health Economics* 4, no. 3 (2018), 404–407;

Ramkumar Janakiraman, Shantanu Dutta, Catarina Sismeiro, and Phillip Stern, "Physicians' Persistence and Its Implications for Their Response to Promotion of Prescription Drugs," *Management Science* 54, no. 6 (2008), 1090.

274 Nabarun Dasgupta, Leo Beletsky, and Daniel Ciccarone, "Opioid Crisis: No Easy Fix to Its Social and Economic Determinants," American Journal of Public Health 108, no. 2 (2018), 182.

275 Nabarun Dasgupta, Leo Beletsky, and Daniel Ciccarone, "Opioid Crisis: No Easy Fix to Its Social and Economic

- "structural factors [such] as lack of economic opportunity, poor working conditions, and eroded social capital in depressed communities, accompanied by hopelessness and despair"[276]

(144) Professor Rosenthal previously explained the importance of analyzing confounding factors in a declaration in the *Neurontin* litigation (among the litigation she describes in her report as "[m]ost relevant to the current matter")[277]

> **The overarching issue that derails Dr. Argenbright's theory** of the value of the data in question **relates to causal inference**…As summarized by one of the seminal references in research design, **inference about a cause and effect relationship requires** the following three conditions: (1) covariation: that is, a change in the cause must relate to a change in the effect; (2) temporal precedence of the cause relative to the effect; and (3) **no plausible alternative explanations. In this instance, the third condition for valid causal inference is highly problematic**…If a patient improves or worsens, how can Neurontin's role be distinguished from the effects of:
>
> - patient characteristics, in particular, those that led a physician to prescribe Neurontin (i.e., selection effects),
> - The natural process of the underlying condition,
> - over-the-counter medications,
> - comorbid conditions, or
> - entirely unrelated factors, such as environmental irritants?"[278]

Below I provide a few examples of factors that Professor Rosenthal did not account for in her models that potentially explain the variation in opioid prescription-based MMEs over time or across counties. Without having accounted for these and other potentially relevant factors, Professor Rosenthal cannot conclude reliably that manufacturer detailing caused opioid MMEs.

(145) In Figure 38, I plot the growth trends for both opioid and non-opioid prescriptions. Though there are more than ten times as many non-opioid prescriptions written as opioid prescriptions, the relationship is readily apparent when the axes are adjusted for comparison. During the period 1993–2010, which roughly corresponds to the first two periods in Professor Rosenthal's direct model, the correlation between the two is 0.99—a strong indicator that the two are interrelated. Even if one were to analyze

Determinants," American Journal of Public Health 108, no. 2 (2018), 182.

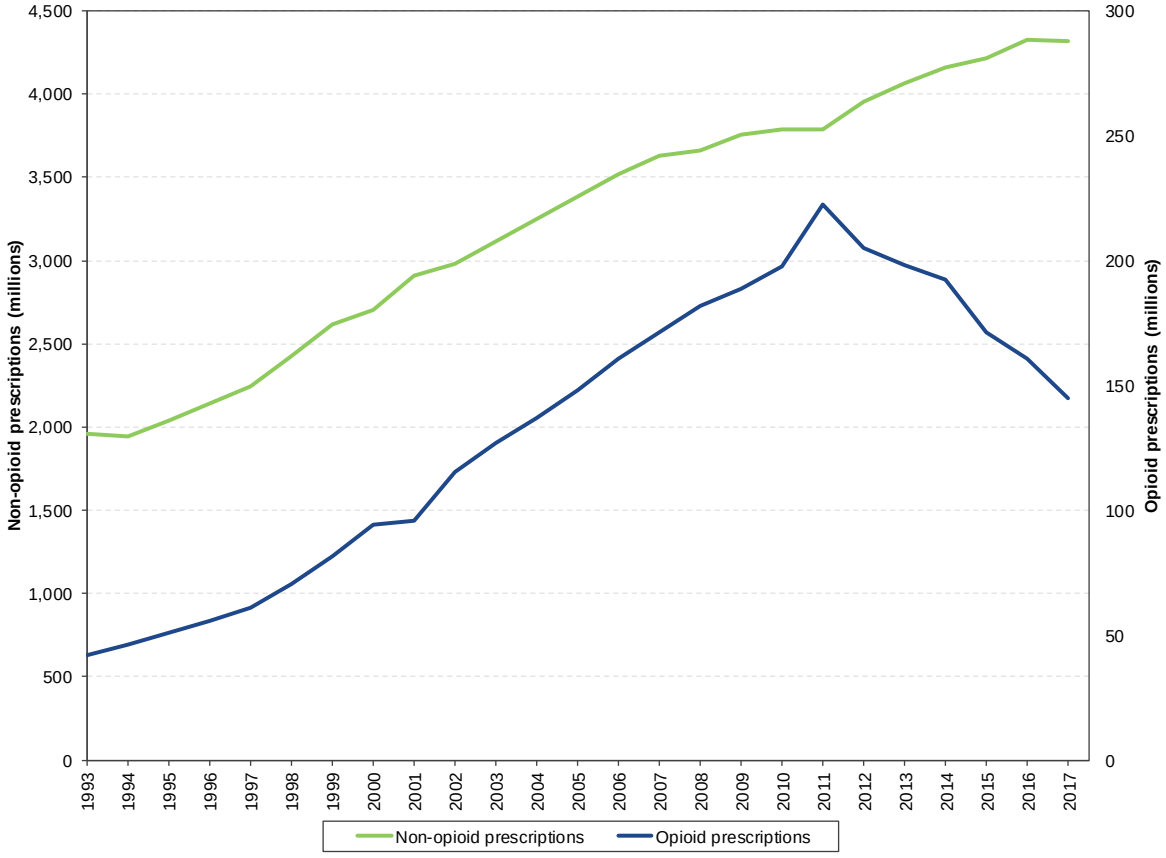
[276] National Academies of Sciences, Engineering, and Medicine et al., "Pain management and the opioid epidemic: Balancing societal and individual benefits and risks of prescription opioid use," The National Academies of Sciences, Engineering, and Medicine (2017), 41.

[277] Rosenthal Rep. ¶ 2.

[278] Declaration of Meredith Rosenthal, In re Neurontin Marketing, Sales Practices, and Products Liability Litigation, MDL Docket No. 1629, Master File No. 04-10981, (D.Ma. September 14, 2006) ¶ 11.

the entire period from 1993–2017 (which includes Professor Rosenthal's third period, and the period in which Professor Cutler has identified the existence of factors designed to limit opioid prescribing), the correlation is 0.92. This relationship is unlikely to be causal: there is no reason to believe that promotion of opioids itself drives prescriptions for unrelated conditions. Thus, this relationship is a strong indicator that some other factor unrelated to opioid promotion is causing both opioid and non-opioid prescriptions to increase (e.g., increased insurance coverage, increased proclivity of physicians to prescribe medication, introduction of new products, etc.). This analysis is similar to the use of a "placebo test" in econometrics, used to verify that a factor hypothesized to cause one outcome does not have a similar effect on an outcome for which the researcher expects no relationship. Professor Rosenthal's models make no attempt to identify this factor or account for it.[279]

Figure 38: Opioid and non-opioid prescriptions, 1993–2017



Source: 2003 HDMA Industry Profile and Healthcare Factbook; 87th Edition HDA Factbook: The Facts, Figures and Trends in Healthcare (2016–2017); 89th Edition HAD Factbook: The Facts, Figures and Trends in Healthcare (2018–2019). Non-opioid prescription data were not available for 2003–2005. I linearly interpolate non-opioid prescribing for these years.

[279] Susan Athey and Guido W. Imbens, "The State of Applied Econometrics: Causality and Policy Evaluation," *Journal of Economic Perspectives* 31, no. 2 (2017), 3–32.

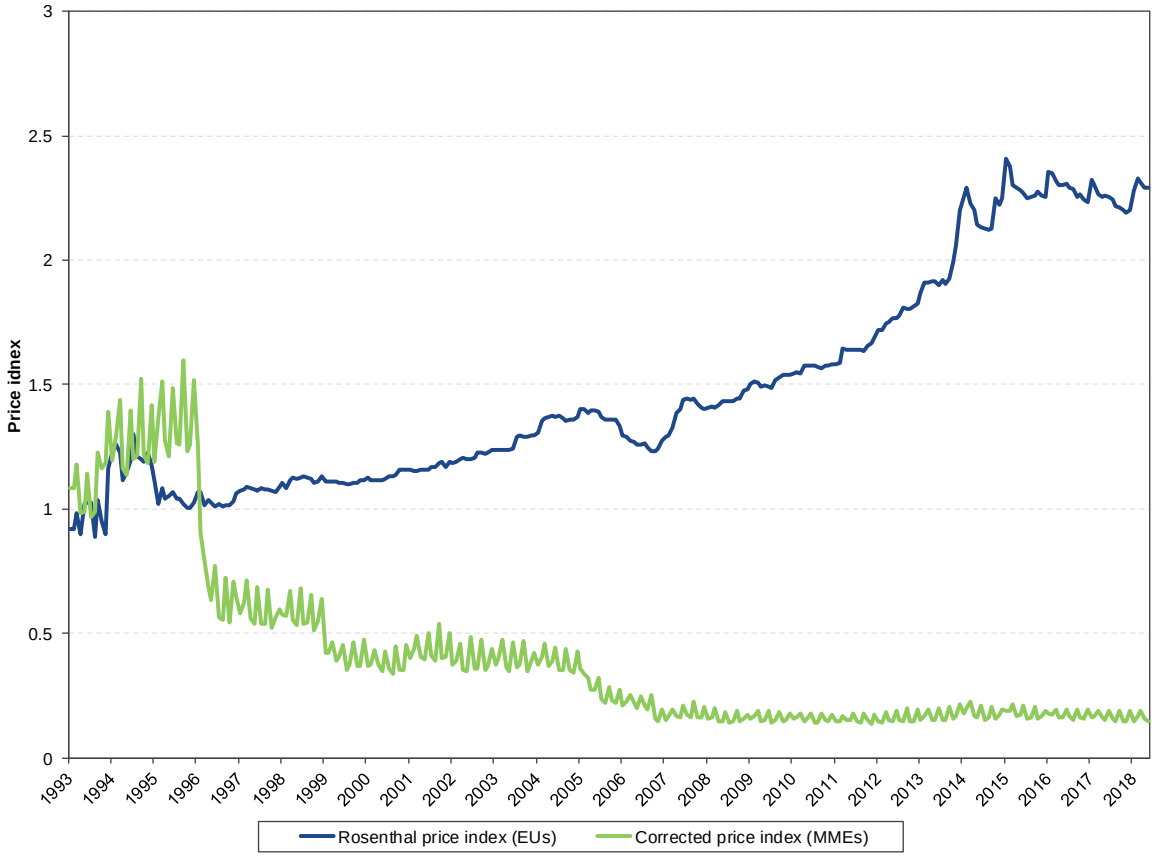
(146) The one variable Professor Rosenthal does attempt to account for in her direct model is price, and she notes "[t]he price index…is statistically significant and in the expected direction (higher prices lead to lower MMEs)."[280]

As Professor Rosenthal's price index increases through time, as seen in the blue line in Figure 39, her models predicts a corresponding decrease in MMEs—the net effect of which is to attribute an even greater share of the actual increase in MMEs to manufacturer promotion. But this prediction is the result of an error in Professor Rosenthal's calculation of the price index.[281] Correcting this error demonstrates that the price index is actually falling through the period in which MMEs are increasing. Theoretically, falling prices would at least in part explain expanding MMEs.

[280] Rosenthal Rep. ¶ 70.

[281] Professor Rosenthal measures the average price per extended unit, and finds an increasing price as more extended release products are introduced, which involve higher MMEs and longer duration associated with few units. But because Professor Rosenthal is attempting to explain changes in MMEs, the correct price index would use the price per MME.

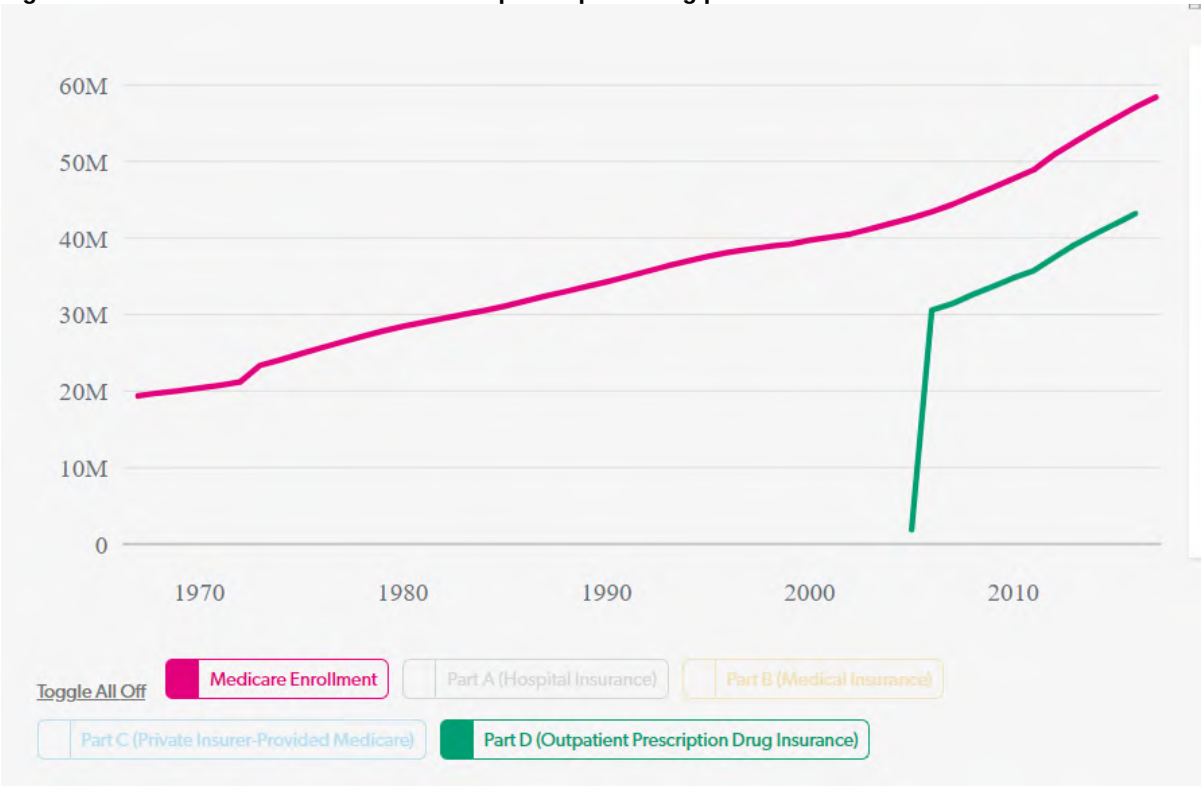
Figure 39: Rosenthal actual and corrected price indices



Source: Rosenthal backup data.

(147) Both of Professor Rosenthal's models also fail to account for changes in prescription drug coverage, which would be expected to increase prescribing. Professor Rosenthal's indirect model does include a broad measure of percent insured, but this is insufficient for two reasons. First, it fails to consider changes in formulary status and utilization management controls (step therapy, prior authorization, quantity limits, etc.) that influence the types and volumes of products each insurance plan will reimburse. I understand Mr. Lieberman has discussed these types of factors in more detail in his report. Second, Professor Rosenthal's measure of insurance coverage examines *medical* insurance, not *prescription drug coverage*. The importance of this distinction is illustrated in Figure 40 below. Enrollment in the Medicare medical benefit, represented by the pink line, has grown at a steady pace since 1970. Medicare retail pharmacy benefits were not provided until 2006, at which point approximately 30 million beneficiaries enrolled (as shown in the green line). Professor Rosenthal's measure of insurance is based on the equivalent of the pink line and fails to account for the large increase in drug coverage that occurs during the same period opioid prescribing is increasing.

Figure 40: Medicare medical enrollment vs. prescription drug plan enrollment



Source: "Medicare Enrollment: Type of enrollment," USA Facts, available at https://usafacts.org/metrics/55637?breakdown=55540&metrics=%7B%2255540%22%3A%5Btrue%2Cfalse%2Cfalse%2Cfalse%2Ctrue%5D%7D

(148) The effects of omitted variables are particularly pronounced in Professor Rosenthal's indirect model, in which she attributes to manufacturers ~50% more opioid MMEs than in her direct model.

VI.D. Professor Rosenthal's "under-treated pain" analysis ignores FDA-approved and other uses of opioids that are potentially appropriate

(149) Professor Rosenthal's "under-treated pain" analysis considers, in reference to Plaintiffs' clinical experts, only a narrow set of appropriate uses of opioids. This set excludes other uses of opioids that I understand are FDA approved and that I understand may be otherwise clinically appropriate under prevailing medical standards. Professor Rosenthal purports to calculate a "[m]aximum [p]ercent of MMEs [e]xplained by [c]linically [j]ustifiable [u]ses," defined as end-of life cancer patients, trauma patients, and surgery patients.[282] She does this by defining inputs that measure volume, a daily dose of MMEs, and a duration of treatment, for each of those three categories (e.g., an end-of-life cancer patient is permitted 64 days of treatment at 80 MMEs per day). She also conducts a "sensitivity" that

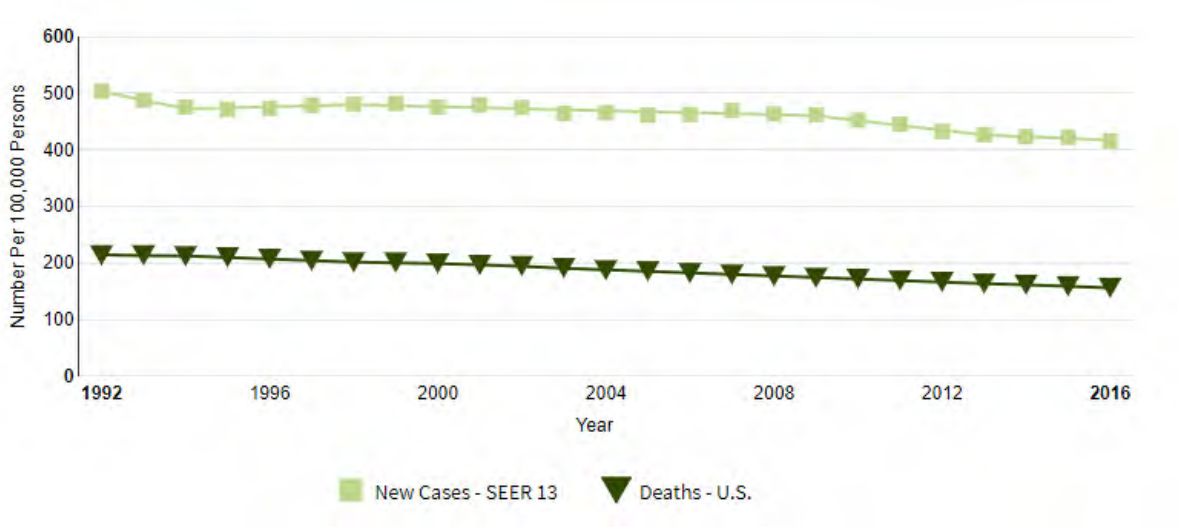
[282] Rosenthal Rep. ¶ 100, Table 6.

increases her calculated MMEs for "under-treated pain" by 50%, which she claims allows for "any input [to] increase[] by 50% (or smaller increases in several inputs that yielded an overall increase of 50%...)."[283]

(150) Though Professor Rosenthal describes her analysis as an "upper bound" and notes that she allows "any input [to] increase[] by 50%," her approach is particularly sensitive to changes to how her inputs are defined.[284] For example:

- If it were determined that *all* cancer patients were eligible for opioid treatment instead of only those in the final two months of life, her sensitivity would have to allow more than a 100% increase in the number of cancer patients, as shown in Figure 41 (and would presumably also have to allow the *duration* of treatment to increase beyond the two months she allows). As Figure 41 compares only *new cases* to mortality, the real increase may be much larger than 100%.

Figure 41: CDC cancer deaths and new cases by year



Source: "Cancer Stat Facts: Cancer of Any Site," National Cancer Institute, https://seer.cancer.gov/statfacts/html/all.html

- If it were determined that a more expansive category of trauma visits were necessary, Professor Rosenthal's model might similarly require a sensitivity larger than 50%. To illustrate, I identify emergency department visits involving diagnoses relating to "trauma," "fracture," "sprain," "injury," or "open wound." If these emergency visits required opioid therapy, trauma visits would increase by 72-82%.

283 Rosenthal Rep. ¶ 101.

284 Rosenthal Rep. ¶¶ 92–93 fn 121.

Figure 42: Trauma visits not captured by Professor Rosenthal's analysis

Year	Trauma visits (Rosenthal)	Trauma visits (adjusted)	Percent increase
2014	21,340,310	38,386,731	80%
2013	21,082,463	38,035,529	80%
2012	21,682,661	39,402,930	82%
2011	21,581,931	38,751,128	80%
2010	21,896,672	38,828,309	77%
2009	21,439,290	37,692,832	76%
2008	21,682,517	38,053,364	76%
2007	21,473,036	37,901,281	77%
2006	21,559,556	36,769,881	71%

Source: HCUP Emergency Department National Statistics. Diagnoses--Clinical Classification Software (CCS), All-Listed Diagnosis: #207 Pathological fracture, #225 Joint disorders and dislocations, trauma-related, #226 Fracture of neck of femur (hip), #227 Spinal cord injury, #228 Skull and face fractures, #229 Fracture of upper limb, #230 Fracture of lower limb, #231 Other fractures, #232 Sprains and strains, #233 Intracranial injury, #234 Crushing injury or internal injury, #235 Open wounds of head, neck, and trunk, #236 Open wounds of extremities, #239 Superficial injury, contusion, #244 Other injuries and conditions due to external causes, #662 Suicide and intentional self-inflicted injury, All ED Visits.

- If it were determined that opioid therapy were appropriate for trauma visits to urgent care centers or facilities other than emergency departments, Professor Rosenthal's estimates could also understate the maximum "appropriate" amount of MMEs. A recent study of commercial claim lines found that "urgent care centers showed an increase in claim lines of 1,725 percent—a growth rate more than seven times that of ER claim lines (229 percent)" during the period 2007-2016.[285]

(151) Professor Rosenthal also excludes from her analysis treatment for several conditions that on the face of Kadian's label appear to have been approved by the FDA. For example, the Kadian label says: "Kadian is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, **long-term** opioid treatment."[286] Professor Rosenthal's analysis does not allow for a single Kadian prescription for "long-term opioid treatment." Including these FDA approved label uses in Professor Rosenthal's model would increase the percentage of MMEs "explained by clinically justifiable uses."

(152) I understand that Dr. Warfield has opined that opioid pain medications can be appropriately prescribed in a wider range of circumstances than those included in Professor Rosenthal's analysis. Further, even for the limited categories of patients Professor Rosenthal does include, I understand Dr. Warfield's opinions suggest Professor Rosenthal's interpretation of them is too narrow. For example, I understand Dr. Warfield opines that opioids may appropriately be used to treat non-end of life

[285] FAIR Health, "FH Healthcare Indicators and FH Medical Price Index: A New View of Place of Service Trends and Medical Pricing," 2018, p.2, available at https://s3.amazonaws.com/media2.fairhealth.org/whitepaper/asset/FH%20Medical%20Price%20Index%20and%20FH%20Healthcare%20Indicators--whitepaper.pdf.

[286] U.S. Food and Drug Administration, "Kadian drug label." Allergan USA, Inc. (2018), available athttps://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020616s061s062lbl.pdf.

cancer patients as well as many more types of trauma patients. Professor Rosenthal acknowledges that certain chronic pain and malignant cancer conditions may require opioid treatment and purports to capture certain "other conditions [that] may be appropriately treated with opioids," but she offers no measure of predicted volume associated with these other conditions or evidence that her 50% sensitivity would sufficiently account for them.[287]

(153) Though I have not undertaken an assessment of each of Professor Rosenthal's inputs, if any—diagnoses categories, volume, appropriate dosage, or appropriate days of supply—are found to be incorrect, her model would likely significantly understate the appropriate level of pain treatment and would therefore not allow her to assess whether "under-treated pain" has contributed to increased MMEs.[288]

VI.E. Professor Cutler's and Professor Gruber's analyses relating opioid shipments to harm ignore myriad other factors

(154) Similar to Professor Rosenthal, Professor Cutler and Professor Gruber also claim a causal relationship between shipments and opioid-related harm.[289] But like Professor Rosenthal, both ignore a number of confounding factors that likely relate to opioid shipments, opioid harm, or both. Indeed, Professor Cutler acknowledges as much with respect to his indirect model—but the statement is just as true for his direct model.[290]

> The indirect regression attributes the entirety of unexplained opioid-related mortality to shipments. To the extent that other factors not modelled in the "baseline" regression contributed to increases in opioid mortality, the indirect approach has the potential to overstate the impact of defendants' actions.[291]

(155) One factor Plaintiffs' experts fail to control for is the focus of the paper on which Professor Cutler based his model. In that paper, Professor Anne Case and Professor (and Nobel laureate) Angus Deaton analyze "deaths of despair" and the recent increase in drug overdoses, suicides, and alcohol.[292] They argue that present economic conditions do not explain increased mortality, and

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287 Rosenthal Rep. ¶¶ 92–93 fn 121.

288 Professor Rosenthal also had access to insurance claims data with which to analyze individual prescriptions to determine, for example, the frequency of prescriptions in Cuyahoga and Summit county associated with trauma, surgery, and end-of-life cancer, but does not appear to have examined these data. Professor Rosenthal does claim her analysis "can be applied at the county level" but her analysis merely "multiplie[s] by county populations/100,000 persons…to estimate county-level trauma incidents" which does not actually account for county-level variation in clinical needs. Rosenthal Rep. ¶ 102, Appendix D8.

289 Cutler Rep. ¶ 26; Gruber Rep. ¶ 16.

290 The *effect* of omitting such factors would manifest in different ways for the direct and indirect model.

291 Cutler Rep. fn. 53

292 Anne Case and Angus Deaton, "Mortality and morbidity in the 21st century," *Brookings Papers on Economic Activity*,

instead attribute such deaths to "cumulative disadvantage" from a variety of long-term factors that would not be captured by Professors Cutler and Gruber's short-term economic variables in their models. Professor Cutler commented on the paper in agreement:[293]

> In their earlier paper, Case and Deaton suggested that the ready availability of opioid drugs might have exacerbated the increased mortality, especially that resulting from accidental overdoses. In their current paper, their emphasis has changed a bit. **Rather than emphasizing the supply of pills, they now focus on the social and economic circumstances that lead people to take them.**
>
> Their overall suggestion is very much in the tradition of Émile Durkheim (1897): People despair when their material and social circumstances are below what they had expected. This despair leads people to act in ways that significantly harm their health. This may have a direct impact on death through suicide, or an indirect impact through heavy drinking, smoking, drug abuse, or not taking preventive medications for conditions such as heart disease. At root is economic and social breakdown.
>
> **This explanation is certainly correct. There is no way to understand the mortality pattern without considering the sources of despair, and the sources of despair must be very deep-seated indeed.** Case and Deaton discuss where this despair may be coming from, and I suspect there is merit in their discussion here as well. That said, **it is extremely difficult for researchers to get at all the aspects that lead individuals to be living a life that they value less than one would hope they would.** Case and Deaton suggest that despair starts early in life, at the time of entering the labor force or before, as expectations about what a "middle-class life" should involve. They **distinguish this from a theory that focuses only on current income, which they say cannot explain all the data** because the median incomes of blacks and Hispanics have been trending in parallel to those of white non-Hispanics; yet these groups have not seen the worsening mortality rates experienced by white non-Hispanics. **Again, I am tempted to believe this**, though the evidence for any particular view about how expectations are formed and what income shocks imply is not as clear as one would like it to be. (Emphasis added.)

(156) In his deposition, Professor Cutler again admitted that "the theory that economic and social breakdown leads people to despair and that they then act in ways that may be harmful, for example,

(2017), 398.

[293] Though Professor Cutler concludes his comment by suggesting a reduction in the supply of opioids, he acknowledges that as a prospective policy solution to address the supply side because "the market has not been able to provide a stable income and social circumstance that people value highly enough to make them want to strive for a long life." Anne Case and Angus Deaton, "Mortality and morbidity in the 21st century," *Brookings Papers on Economic Activity*, (2017), 444–446.

through heavy drinking, smoking, drug abuse, not taking preventive medications, and so on, that that is certainly correct at least in part."[294] Yet, he admitted that his regression models were unable to account for these factors and the impact they had on mortality:

> Q. Just like Case and Deaton, you also don't have data to say whether their theory that these deaths -- increase in deaths in the '90s and 2000s are related to deep-seated social and demographic circumstances?
>
> A. I wish I had the ability as a scholar and a human being to test that. They were unable to test it fully in their work. They showed some correlations. They were unable to test it fully in their work. I wasn't able to -- I did not have access to any data they did not have access to.[295]

Professor Cutler testified that he "is explicitly hoping" other variables in his model account for these characteristics, but that he "cannot give an econometric answer to the question of what impact including such variables would have."[296]

(157) Professor Cutler further testified to a laundry list of variables many of which he "wishe[es] he had the data to measure" but was "not able to include" each of which may "lead the impact of the shipments variable to go up, to go down, or to be the same,"[297] including:

- "long-term declines in marriage rates"
- "rise of cohabitation"
- "rise in out-of-wedlock births"
- "parents living apart from children that they barely know"
- "changing religious practices"
- "share of the population that is living alone"
- "veterans"
- "number of doctors"
- "number of hospitals"
- "eligibility for Medicare Part D"[298]

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294 Cutler April 27 Dep. at 480:14-20.

295 Cutler April 27 Dep. at 485:24–486:11.

296 Cutler April 27 Dep. at 488:4, 558:22-559:14.

297 Cutler April 27 Dep. at 495:19-492:10.

298 Professor Cutler testifies that "the population that is eligible for Medicare Part D is actually included" in his measure of "the elderly population" but this may not appropriately control for Medicare Part D eligibility. As discussed in Section

- "employer-sponsored health insurance"
- "incidence of cancer"
- "mental health"
- "percent of the population that's covered by insurance"
- "trade liberalization"

Professor Cutler does testify that he believes his model will pick up some of the effects of some of these variables, but without the data, he is unable to demonstrate that they are in fact picked up, let alone quantify the effect empirically.

(158) Professor Gruber quotes selectively from a follow up response by Case and Deaton, arguing that in rejecting "the idea that deaths are related to economic conditions from 1999–2015" their paper is consistent with the conclusions of his analysis that availability of prescription opioids, not economic factors, is the driver of the opioid abuse crisis.[299] However, the Case and Deaton response does not argue that economic factors are unimportant, but rather that the drivers involve "much more than economic circumstances and go[] back much further than 1999."[300] Instead, they cite as relevant longer run declines in labor force participation, marriage rates, quality of jobs, opportunity for people without college degrees, and unions, among other factors—none of which Drs. Gruber or Cutler attempt to account for in their models.

(159) Professor Gruber also omits from his characterization Case and Deaton's rejection of availability and cost of drugs as the sole factor explaining mortality. Indeed, they conclude their response by noting, "[t]here is a lot more going on than just the opioid epidemic, including prescription drugs, heroin, and fentanyl, and we continue to believe that the broader epidemic, including opioids, is linked to the longterm decline of working class lives."[301] To support this statement, they point to increasing suicide and alcohol-related mortality, shown in Figure 43, as evidence that factors unrelated to opioid prescribing drive "deaths of despair." And they further criticize the very mortality data and Ruhm adjustment that Professors Gruber and Cutler use in their analyses—as overstating opioid deaths by

VI.B, Medicare Part D was introduced in 2006, and it is not evident that Professor Cutler's measure of the elderly population would appropriately control for the change in individuals with prescription drug coverage over time.

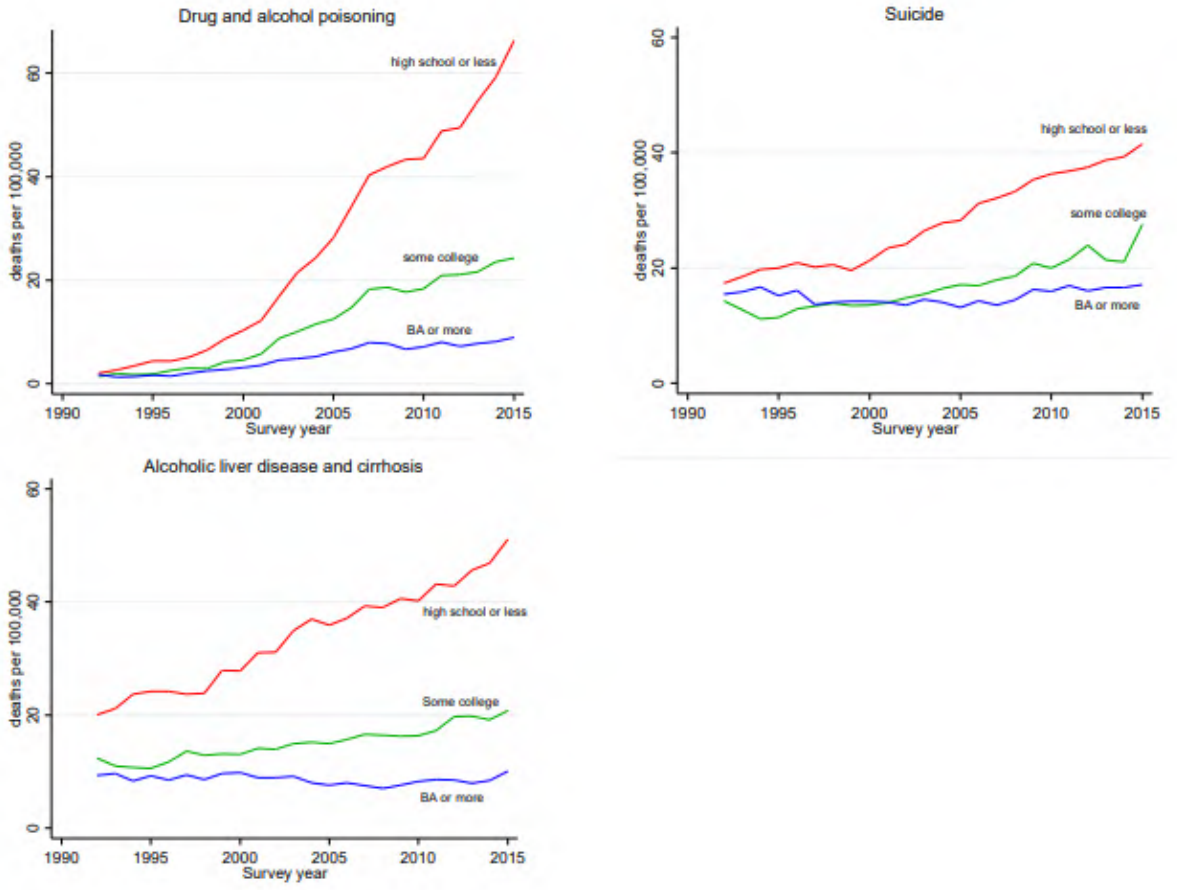
299 Gruber Rep. ¶ 101-103.

300 Anne Case and Angus Deaton, "Deaths of despair redux: a response to Christopher Ruhm," Response to a working paper, January 8, 2018, available at https://www.princeton.edu/~accase/downloads/Case_and_Deaton_Comment_on_CJRuhm_Jan_2018.pdf.

301 Anne Case and Angus Deaton, "Deaths of despair redux: a response to Christopher Ruhm," Response to a working paper, January 8, 2018, available at https://www.princeton.edu/~accase/downloads/Case_and_Deaton_Comment_on_CJRuhm_Jan_2018.pdf

including suicides that would have occurred even in the absence of opioids.[302] Professor Cutler did not make any adjustments to his analyses to account for suicide deaths.[303]

Figure 43: "Deaths of despair," 1992–2015



Source: Anne Case and Angus Deaton, "Deaths of despair redux: a response to Christopher Ruhm," Response to a working paper, January 8, 2018, available at https://www.princeton.edu/~accase/downloads/Case_and_Deaton_Comment_on_CJRuhm_Jan_2018.pdf

(160) Plaintiffs' economic experts' failure to account for the underlying causes of "deaths of despair" causes their indirect models to overestimate the relationship between opioid shipments and mortality—any growth in these factors which is unaccounted for is incorrectly attributed to defendants, as Professor Cutler acknowledges.[304] But Professor Cutler's inability to control for such

[302] Anne Case and Angus Deaton, "Deaths of despair redux: a response to Christopher Ruhm," Response to a working paper, January 8, 2018, *available at* https://www.princeton.edu/~accase/downloads/Case_and_Deaton_Comment_on_CJRuhm_Jan_2018.pdf.

[303] Cutler April 26 Dep. at 296:6–12, 301:1–302:14.

[304] Cutler Rep. fn 53.

factors also highlights a flaw in his direct model, which may establish correlation between mortality and shipments but does not prove causation.[305] His model is incapable of determining whether increases in opioid shipments in fact *cause* increases in opioid mortality, or whether some other underlying factor, such as despair, causes individuals to demand prescription opioids and also to shorten their lifespan, whether through prescription opioids, illicit opioids, alcohol, or suicide.[306]

(161) These same unmeasured factors highlight a flaw in Plaintiffs' experts' theory of a causal relationship between the decline in prescription opioids and the rise of illicit mortality. Though Professors Cutler and Gruber provide evidence of correlation, they again fail to demonstrate causation. Areas with a high demand for prescription opioids are likely to have a high demand for illegal opioids due to these same unmeasured factors. Though some of the increase in illicit mortality may indeed represent prescription drug users shifting to illicit substances as supply of prescription opioids is reduced, Plaintiffs' models fail to demonstrate that those individuals would not have started on illicit substances in the absence of licit opioids. And as Professor Cutler acknowledges, other users of heroin and fentanyl have *never* started on prescription opioids.[307] According to the National Institute on Drug Abuse, "only a small fraction of people who misuse pain relievers switch to heroin. According to a national survey, less than 4 percent of people who had misused prescription pain medicines started using heroin within 5 years. This suggests that prescription opioid misuse is just one factor leading to heroin use."[308] Both experts' models of illicit mortality fail to consider alternative explanations for increased consumption among those users, including increased accessibility that is unrelated to prescription opioid shipments.

(162) This failure to control for other factors that might explain the increased illicit mortality is a critical flaw of Drs. Cutler and Gruber's indirect models. Though both present their illicit models as demonstrating a causal relationship between defendant actions and illicit mortality, they do not measure directly the impact of historical shipments. Both instead make the unsupported assumption that *any* increase in illicit mortality not explained by broad economic and demographic changes *must* be caused by defendant misconduct, while failing to consider other basic economic factors that have a more direct relationship with illicit consumption—namely, supply and price. As shown in Figure 44 below, heroin seizures (a proxy for supply) more than doubled during the period 2010–2014, and continued to rise thereafter. Relatedly, the price of heroin after adjusting for inflation and purity

[305] Professor Cutler argues that his direct model would not need to include these variables because if "there was a substitution from suicide to accidental poisoning then a combined measure of mortality that included them both would not be related to drug shipments at all provided one were looking at all causes of death." Cutler April 26 Dep. at 319:6–11. But because Professor Cutler's model looks only at *opioid*-related mortality his model does not account for this substitution.

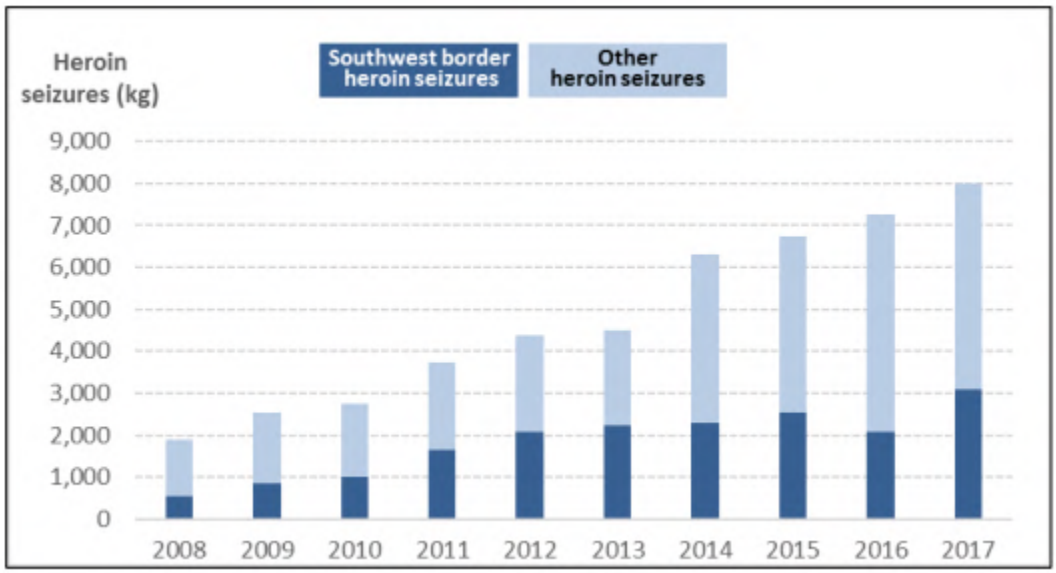
[306] Professor Gruber does assert that "shipments of prescription opioids were a medium through which despair translated to higher deaths," basing this statement on evidence that "deaths grew faster in higher shipment areas." But like Cutler, this is an argument of correlation, not causation. Gruber Rep. ¶ 105.

[307] Cutler Rep. ¶ 62.

[308] *See* National Institute on Drug Abuse, "Drug Facts: Heroin," June 2018, available at www.drugabuse.gov/publications/drugfacts/heroin.

dropped from $622 per gram in 2010 to $486 in 2012 and continued to decline thereafter, as shown in Figure 45. Basic economic theory predicts that increased supply and reduced price would increase consumption of illicit heroin—a more direct link to heroin mortality than the hypothesized relationship to prescription opioid shipments—yet Professor Cutler and Professor Gruber fail to consider either effect in asserting a causal relationship between shipments and illicit mortality.[309]

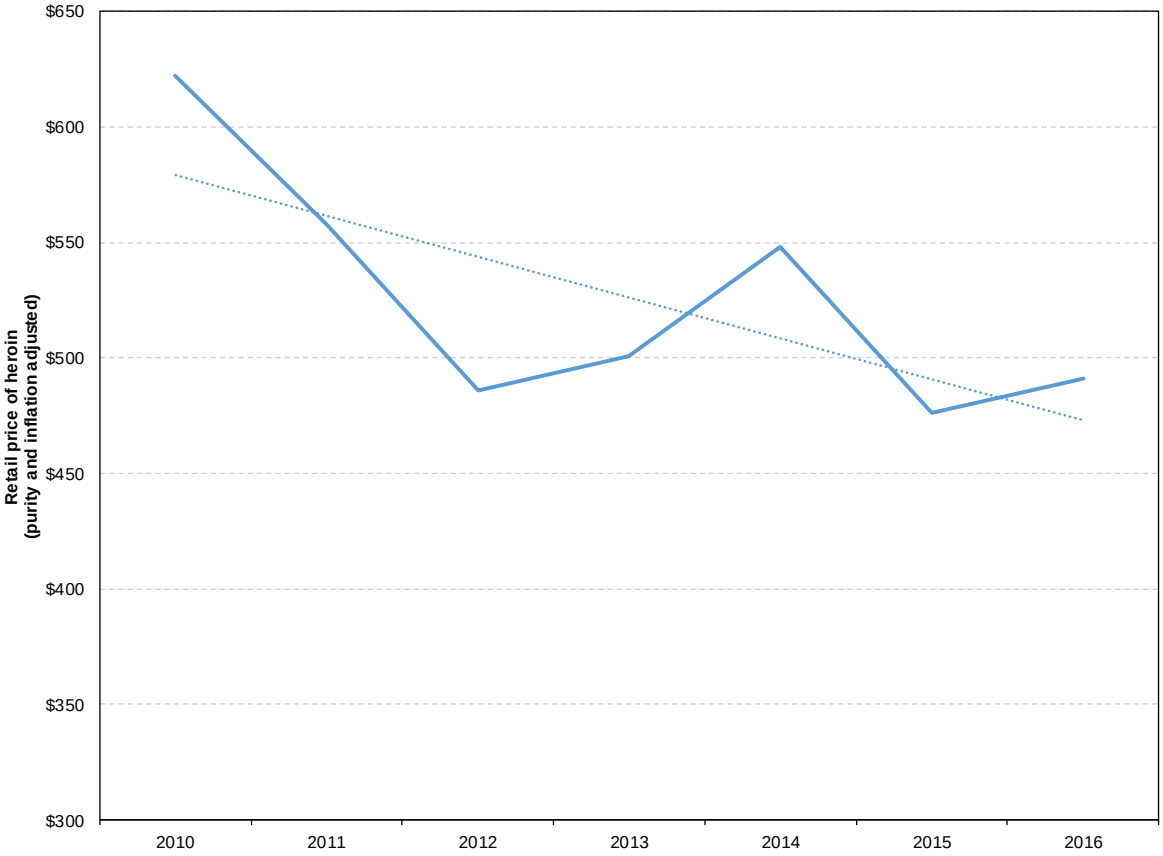
Figure 44: Heroin seized in the United States, 2008–2017



Source: Kristin Finklea, Cong. Research Serv., R44599, Heroin Trafficking in the United States Figure 1 (2019).

[309] Professor Cutler briefly addresses supply-side factors, but concludes that they cannot be observed and asserts that "the presence and sophistication of drug networks is partially a result of opioid shipments prior to 2010" and provides no evidence in support of this assertion. "Q. You cannot quantify the contribution that pre-2010 shipments made to the presence or sophistication of drug networks in Cuyahoga or Summit after 2010? A. Unfortunately we don't have data on presence or the sophistication of drug networks anywhere. Because it's an illegal good, we just don't have that. So there's really no economic way to try and do a quantification of that." Cutler Rep. ¶ 71. *See* Cutler April 27 Dep. at 412:4–12.

Figure 45: Retail price of heroin adjusted for purity and inflation, 2010–2016



Source: 7.5_Standardized_prices_of_cocaine_and_heroin_in_the_United_States_and_Western_Europe.xlsx, United Nations Office on Drugs and Crime, "Heroin and cocaine prices in Europe and USA," available at https://dataunodc.un.org/drugs/heroin_and_cocaine_prices_in_eu_and_usa.

(163) Professor Cutler states that the reduction in heroin price is "not some exogenous change," but rather a response to factors associated with the legal opioid abuse crisis.[310] Economic theory predicts that the relationship between the price of licit and illicit opioids should be positive, all else equal, if the products are substitutes. However, in the post-2010 period, the price of licit opioids arguably increased as states introduced PDMPs and prescribers became more aware of the risks of addiction, and legal opioids became more difficult to obtain. The observation that the price of heroin and other illicit opioids in fact *fell* during this time period, when theory predicts it should have increased if nothing else in the market changed, is therefore consistent with shocks to supply conditions on the illicit side.

(164) Recent studies have identified several such supply side shocks. These include:

[310] Cutler April 26 Dep. at 322:9–14.

- A new form of Mexican heroin, with higher purity[311]
- Synthetic opioids, particularly fentanyl, with much higher potency than morphine and heroin[312]
- Cryptomarkets that facilitate the distribution of illicit opioids around the world and within the US[313]

(165) Professor Cutler views these supply side changes, as well as the sophistication of illegal drug distribution networks, as endogenous responses to demand created by legal opioids. However, he views the demand for legal opioids as driven by supply side factors. He provides no explanation for why he believes legal supply (excess shipments) causes legal demand, which itself creates illegal demand, but dismisses the idea that illegal supply causes (or at least contributes) to illegal demand.

(166) Professors Cutler and Gruber argue that increased demand for illicit opioids post-2010 was caused by existing users of licit opioids, who switched to heroin and other illicit products when legal products became more difficult to obtain or abuse. Shipments of legal opioids have declined, implying fewer new consumers of legal opioids who then may subsequently have switched to heroin. Recent evidence indicates that patients entering substance abuse treatments in 2015 were more likely to initiate opioid use with heroin, rather than legal opioids like oxycodone and hydrocodone.[314] It is therefore unlikely that existing users of legal products continue to drive mortality due to illicit products at a constant rate.

(167) Professor Cutler incorrectly asserts that "prior to 2010, essentially all of the use of opioids was use of legal opioids."[315] Heroin use obviously existed well before 2010, and caused deaths before 2010, as illustrated in Figures III.2-3 of his report. In addition:

- The number of individuals reporting any use of heroin within the past year began trending upwards in 2007[316]

---

311 Daniel Ciccarone, Jeff Ondocsin, and Sarah Mars, "Heroin uncertainties: exploring users' perceptions of fentanyl-adulterated and -substituted 'heroin'," International Journal of Drug Policy 46, no. (2017), 11–15.

312 Daniel Ciccarone, Jeff Ondocsin, and Sarah Mars, "Heroin uncertainties: exploring users' perceptions of fentanyl-adulterated and -substituted 'heroin'," *International Journal of Drug* Policy 46, no. (2017), 13–15.

313 *See* Michael Gilbert and Nabarun Dasgupta, "Silicon to syringe: Cryptomarkets and disruptive innovation in opioid supply chains," *International Journal of Drug Policy* 46 (2017), 160–167.

314 Theodore J. Cicero, Matthew S. Ellis, Zachary A. Kasper, "Increased use of heroin as an initiating opioid of abuse," *Addictive Behaviors* 74 (2017), 64.

315 Cutler April 26 Dep. at 330:2–5.

316 Rachel N. Lipari and Arthur Hughes, "The NSDUH Report: Trends in Heroin Use in the United States: 2002 to 2013," in The CBHSQ Report: April 23, 2015, Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, available at https://www.samhsa.gov/data/sites/default/files/report_1943/ShortReport-1943.html.

- The number of individuals reporting first use of heroin within the past year increased substantially in 2009[317]

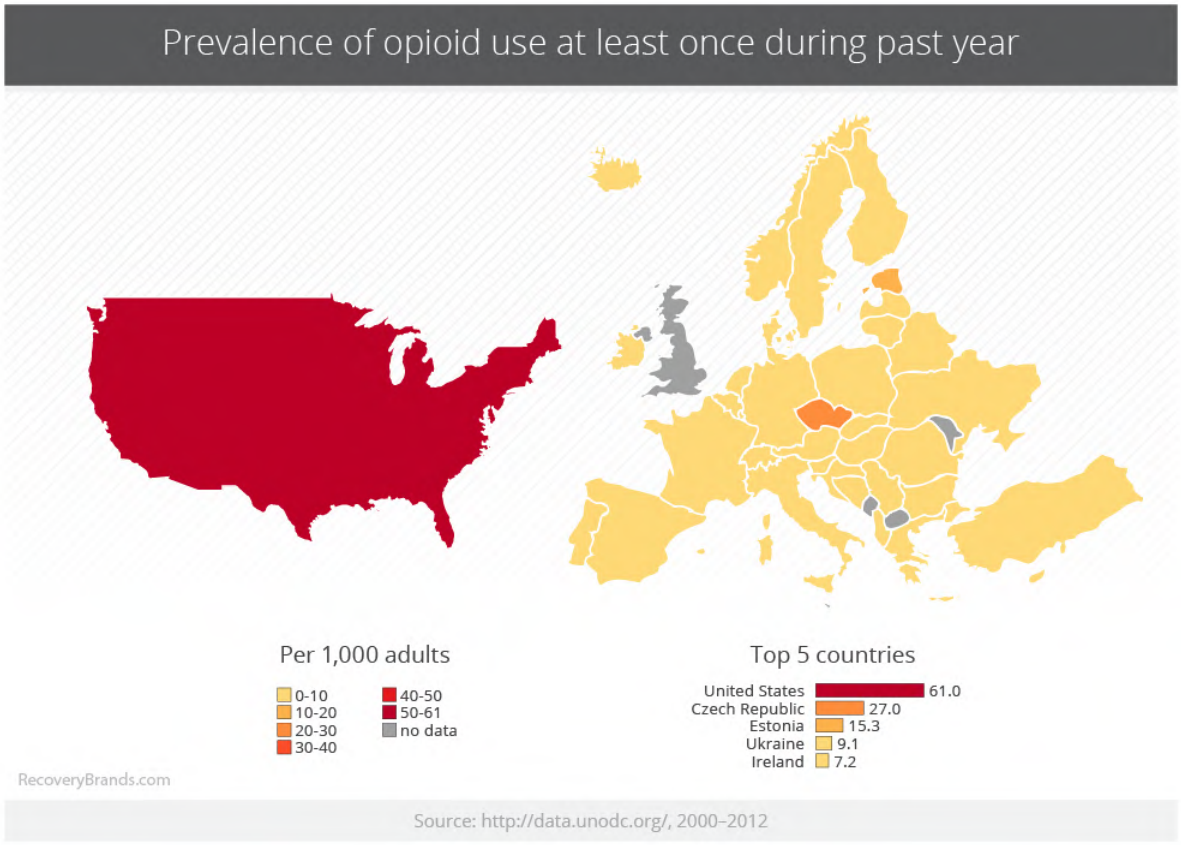
These two facts are inconsistent with the theory that a shift by existing users of legal opioids to heroin and other illegal products caused by 2010 changes on the supply side of legal opioids (reformulation of OxyContin, increased monitoring and enforcement by the DEA, etc.), is solely responsible for the increase in illicit opioid mortality. The increase in illicit use began before those changes, when shipments of legal opioids were still growing.

(168) Professors Cutler and Gruber also fail to consider numerous other explanations for rising mortality, as both acknowledged in their depositions.[318] As shown in Figure 46, European nations have substantially less prescription opioid use than the United States. If this were the sole predictor of opioid mortality, one would not expect to observe the same 2010 increase in illicit opioid mortality as that observed in the United States. But as shown in Figure 47, overdose deaths in the European Union have increased about 30% from 2010 to 2016—a lesser increase than in the United States, but a similar increasing trend over a similar period. Overdoses from fentanyl in the United Kingdom have similarly grown, increasing more than 700% between 2010 and 2017, as shown in Figure 48. This correlation is not causal (overdose deaths in Europe are unlikely to drive overdose deaths in the US), but it is a strong indicator that some factor unrelated to US opioid promotion and shipments, and to corresponding US-based enforcement actions—whether supply and price or something else—is contributing to rising mortality globally.

[317] Rachel N. Lipari and Arthur Hughes, "The NSDUH Report: Trends in Heroin Use in the United States: 2002 to 2013," in The CBHSQ Report: April 23, 2015, Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, available at https://www.samhsa.gov/data/sites/default/files/report_1943/ShortReport-1943.html.

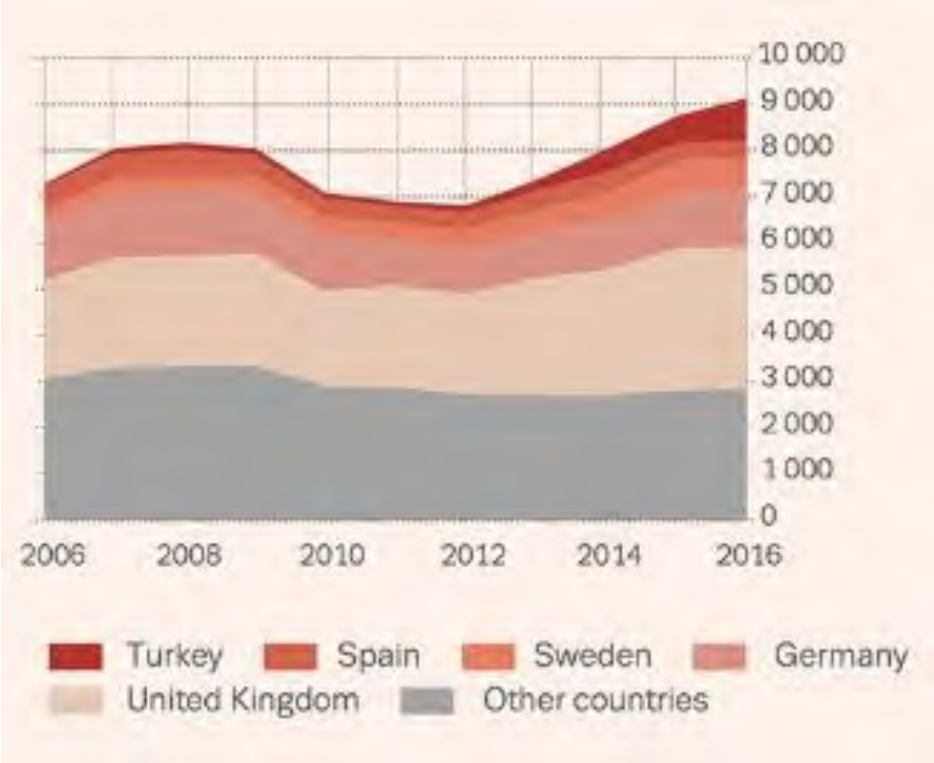
[318] *See e.g.*, Deposition of David Cutler, April 27, 2019 [hereinafter "Cutler April 27 Dep."] at 467–471; Deposition of Dr. Jonathan Gruber, April 25, 2019 [hereinafter "Gruber Dep."] at 229-236.

Figure 46: The prevalence of opioid use is far higher in the United States than in Europe



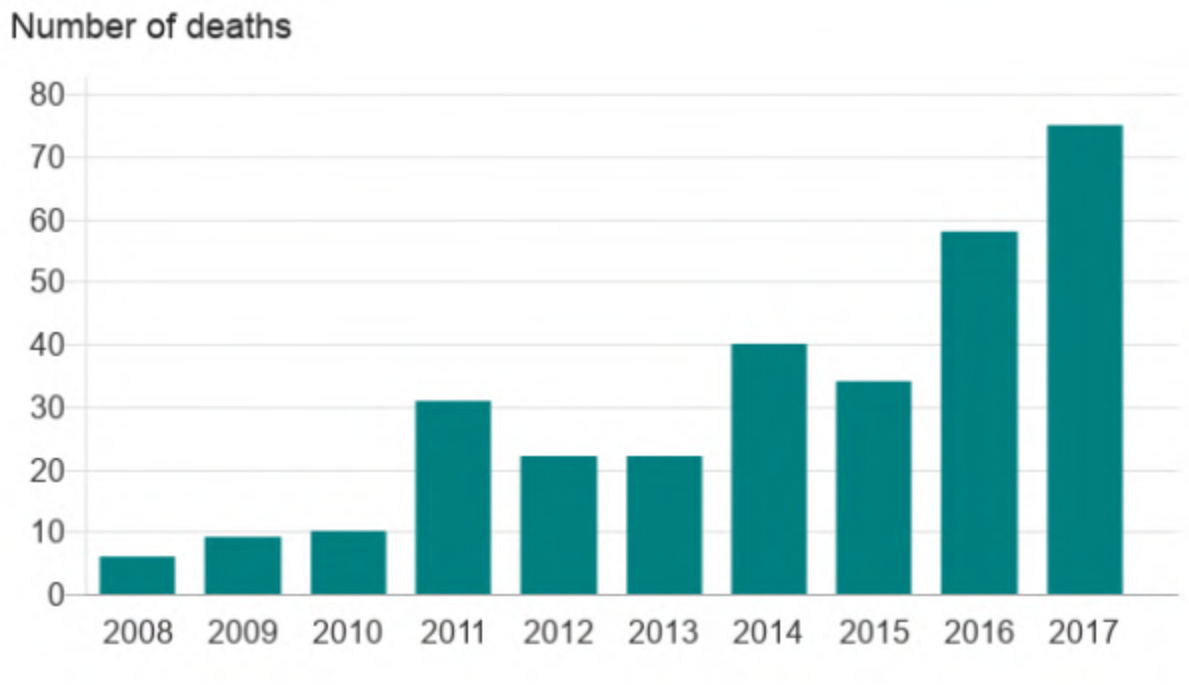
Source: RecoveryBrands, "Drug Use in America vs. Europe," accessed May 1, 2019, available at https://recoverybrands.com/drugs-in-america-vs-europe/assets/images/xprevalence-of-opioid-use-once-year-past-year.png.pagespeed.ic.D9hW2Qci7y.png.

Figure 47: Overdose deaths in EU member states, Turkey, and Norway, 2006–2016



Source: European Monitoring Centre for Drugs and Drug Addiction, "Statistical Bulletin 2018 — overdose deaths," accessed May 2, 2019, http://www.emcdda.europa.eu/data/stats2018/drd_en.

Figure 48: Fentanyl deaths in the UK, 2008–2017



Source: BBC News, "Fentanyl and cocaine drug deaths rise," August 6, 2018, available at https://www.bbc.com/news/uk-45083167.

(169) While Professor Cutler asserts a link between county-level mortality from licit opioids and that from illicit, this link is not evident in hospitalizations for overdose at the level of US Census divisions, nor at the level of race or age groups within those divisions. When comparing hospitalizations from prescription opioid overdose (POD) to those of heroin overdose (HOD), Unick and Ciccarone (2017) find that POD trends are fairly uniform across Census divisions, but HOD trends are not. POD and HOD hospitalizations show different age distributions as well as differences across races.[319] For example, POD hospitalization rates are relatively low for Hispanics overall, and HOD hospitalization rates for Hispanics are low in most Census divisions. However, they are high and increasing in New England. POD hospitalization rates tend to be higher for people over 50, but HOD hospitalization rates are higher for those under 35. These patterns suggest a more nuanced story than the simple vector of legal shipments before 2010 driving increased illicit mortality after 2010 through the creation of "thick markets": the customers in these markets are sometimes very different, and a direct link is not as clear as described in Professor Cutler's report.

[319] George Unick and Daniel Ciccarone, "US Regional and Demographic Differences in Prescription Opioid and Heroin-Related Overdose Hospitalization," *International Journal of Drug Policy* 46 (2017), available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5722230/pdf/nihms890776.pdf.

(170) Similarly, mortality caused by prescription opioids exhibits a different pattern than mortality caused by heroin and synthetic opioids. The latter are much more pronounced in the eastern US, while prescription opioid mortality is highest in Appalachia and the Midwest.[320]

(171) Professor Cutler also purports to calculate the "share of harms attributable to opioids" by evaluating five categories of alleged harm: crime, addiction and mental health, children's and family services, juvenile court activity, and medical examiner activity.[321] For this analysis, he relies upon national, state, and local statistics, and he does not even attempt to model causation. Yet these statistics suffer from the same problem as his models—merely measuring that a harm is "opioid-related" does nothing to establish causality, nor to prove that the same harm would not have occurred even in the absence of opioids. Indeed, Professor Cutler acknowledges as much in his report:

> NDIC counts only 10 percent of crimes committed under the influence of drugs as "drug crimes," assuming that 90 percent of such crimes also would have been undertaken in the absence of drugs."[322]
>
> …
>
> Unlike **crime or foster care placements**, which are harms that one would expect **would exist at some level even without opioids**, there is no reason to expect there would be opioid related deaths in the absence of supplies of prescription opioids and illegal substitutes.[323]

(172) Professor Cutler also testified that his analyses fail to consider whether the harm would have occurred in the absence of opioids:

- With respect to crime, Professor Cutler testified that he "assumes there would be no substitution into other types of activities which would have also led to the crime."[324]

[320] Matthew V. Kiang, Sanjay Basu, Jarvis Chen, and Monica J. Alexander, "Assessment of Changes in the Geographical Distribution of Opioid-Related Mortality Across the United States by Opioid Type, 1999–2016," *JAMA Network Open* 2, no. 2 (2019), 4–7.

[321] Cutler Rep. Section IV.

[322] Cutler Rep. fn 20.

[323] Cutler Rep. ¶ 47 (emphasis added).

[324] Cutler April 26 Dep. at 227:19–22. Professor Cutler does attempt to account for this problem when measuring his crime statistic by running a separate crime regression, but does not "do any confirmatory analysis" on his other areas of harm. Moreover, his crime regression suffers from the same flaws as his direct mortality regression in that it fails to account for myriad factors that could explain geographic variation crime, several of which he acknowledges in his deposition testimony. Cutler April 27 Dep. at 568–569.

- Regarding addiction and mental health activity attributable to opioids, Professor Cutler testified that he "did not assume any offset, that is [he] did not assume that people would were addicted to opioids if there had been no opioids would have been addicted to anything else."[325]
- Regarding child services, he testifies that his analysis assumes "the removal would not have occurred had the family not been using opioids" despite the statistic he relies on merely reporting the "percent of children taken into custody in 2015 [who] had parents who were using opioids at the time of removal."[326] Indeed, Professor Cutler testified that the report "doesn't show whether these parents were using other substances at the time" and "doesn't say whether they were sent to jail for any other reason."[327]
- Regarding mortality, he testifies that "if there is an opioid that was listed in the toxicology report but also other drugs" then "that would count as an opioid-related autopsy" regardless of the relative volume and further, that he did not "separate out accidental drug deaths from drug suicides."[328] As a result, "it's necessarily the case that some of the suicides end up in the percentage of harms that [Professor Cutler is] attributing to the defendants."[329]

(173) Finally, Professor Cutler fails to properly account for the benefits associated with increased opioid MMEs in his models and harm calculations. He acknowledges that he does not "look at the benefits in addition to the costs" and instead is only "looking at harms."[330] Professor Cutler also describes the potential benefits, though incorrectly believes that his model would account for some of these:

> If it had been the case that treating people's pain improved their quality of life to a degree sufficient that their mortality fell, and that, therefore, they lived longer and so on and so forth that would – and there was no crime and no child welfare issues and so on, that would show up in the models, in mortality models it would show up as a reduction in deaths associated with increased shipments…There's absolutely nothing in the analysis that prejudges that these will find harmful effects of opioid shipments as opposed to favorable effects of opioid shipments.

(174) However, Professor Cutler's model measures only the *opioid* mortality rate, so it necessarily prejudges. The potential benefits Professor Cutler outlines would not manifest through a reduction in *opioid* mortality, they would appear as a reduction in other forms of mortality and increases in other

325 Cutler April 26 Dep. at 241:11–15.
326 Cutler April 26 Dep. at 259:12–260:24.
327 Cutler April 26 Dep. at 269:5–12.
328 Cutler April 26 Dep. at 288:10–296:18.
329 Cutler April 26 Dep. at 312:4–7.
330 Cutler April 26 Dep. at 150:17–23.

forms of quality of life. Because his model fails to measure potential offsetting benefits, it measures gross harm, not net harm.

VI.F. Adjusting Professor Cutler's analysis to examine prescription MMEs instead of shipments reduces his estimated harm by nearly half

(175) In calculating his percentage of opioid mortality attributable to defendant misconduct, Professor Cutler relies on the results of Professor Rosenthal's preferred direct model, which he mistakenly describes as estimating the "share of **shipments** due to defendants' misconduct."[331] This reliance mischaracterizes Professor Rosenthal's analysis, which purports to identify the percentage of MMEs—measured using IQVIA *prescription* data—that are caused by manufacturer defendant conduct. In this section, I demonstrate that merely substituting the *prescription*-based MMEs that Professor Rosenthal used in her analysis for *shipment*-based MMEs reduces Professor Cutler's damages estimate by nearly half.

(176) In his report and his deposition, Professor Cutler describes his model as measuring the impact of *shipments* rather than *prescriptions*. Professor Cutler also describes the effect of this difference, noting that (a) his shipment measure can include products acquired by means other than a prescription (e.g., stolen or from friends or family), and (b) he does not identify which portion of those shipments are attributable to defendants, instead relying on an input from Professor Rosenthal.

> Q. Just to be clear, you didn't study the impact on mortality that doctors' prescriptions had at any point in time, correct?
>
> A. To the extent that the shipments that we're picking up here are a result of doctors' prescriptions, then they are, in fact, here, so -- as opposed to **other ways of obtaining MMEs, either stolen or through borrowing from friends or family**. So this is a summary of all the prescriptions sort of weighted up in terms of the MMEs that were shipped.
>
> Q. But to be clear, in your model you don't attribute any of the harms associated with the shipments to the doctors that actually wrote the prescriptions, right?
>
> A. **This model is not designed to say how much of this shipment is a result of different factors.** This is designed to give the effect of the shipments on mortality. That's then used in conjunction with Professor Rosenthal's estimates to say what is the impact of the misconduct of the defendants. So **anything about misconduct of a particular person or organization would show up in the input from Professor**

[331] Cutler Rep. ¶ 105 (emphasis added)

> **Rosenthal**, and I would not want to -- it wouldn't make economic sense to include them in this model.[332]

(177) In contrast, Professor Rosenthal describes her analysis as measuring "the extent to which the sale of **prescription** opioids…was caused by any quantum of the Defendants' promotional efforts that counsel can prove was unlawful."[333] She relies on IQVIA NPA data, which "tracks sales of prescription drugs in retail outlets."[334] Because of this, her analysis appropriately does not consider "stolen or…borrow[ed]" opioid shipments unrelated to defendant promotion as part of her percentage.[335]

(178) Professor Cutler also acknowledges that the difference in measurement could affect his regression coefficient, depending on whether non-prescription shipments are associated with more harms, but incorrectly believes he lacks the data to test this.[336]

> Q. So what if -- what if we convert the prescriptions to milligram equivalents, milligram morphine equivalents, my question is, if you had run your direct regression using prescription activity, do you believe that it would result in substantially the same coefficient in relation to driving opioid mortality?
>
> A. I don't want to hazard a guess as to what the coefficient would be. In general -- and I also want -- would want to compare the two series. The ARCOS data includes, I believe it is six different categories of where drugs are shipped to. The prescriptions may only capture one of those areas or potentially more than one. In order to judge those two, which, first off, I don't -- I don't have an econometric way to estimate whether they would be similar. But in order to judge those two, **what I would want to see is which one is picking up more of what we think would be the shipments that would be associated with harms, those that come from prescriptions themselves or those that come from all shipments to all the retail categories that are picked up in ARCOS.**[337]

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[332] Deposition of David Cutler, April 27, 2019 [hereinafter "Cutler April 27 Dep."] at 522:22-524:2 (objections omitted) (emphasis added).

[333] Rosenthal Rep. ¶ 11 (emphasis added).

[334] Rosenthal Rep. ¶ 51.

[335] To illustrate the effect of this misunderstanding, consider a hypothetical scenario in which 25% of shipments are "stolen or…borrow[ed]" and Professor Rosenthal's percentage impact attributable to alleged misconduct is 50%. If that percentage impact were of shipments, 50% of shipments would be attributed to defendant misconduct. But because that percentage impact is of prescriptions, only 37.5% of shipments are attributed to defendant misconduct (50% * 75%), with an additional 25% having been removed as non-prescription product that is unrelated to promotional activity.

[336] Cutler April 27 Dep. at 647:24–648:7

[337] Cutler April 27 Dep. at 645:1-646:3 (objections omitted) (emphasis added).

(179) Figure 49 reproduces Professor Cutler's Figure III.10 from his report that shows that his measured "Percent Impact on Mortality" ranges from 21.1%–25.9% over the period 2006–2010. In Figure 50, I recreate Professor Cutler's impact percentages by running his model using IQVIA *prescription* data measured in MMEs instead of shipments. Without attempting to correct any other flaws and without conceding that his regression model appropriately supports a causal conclusion with respect to any measured variable (it does not), substituting prescription data alone reduces his impact percentages by almost half, to a range between 12.5% and 15.7%.[338]

Figure 49: Professor Cutler's Figure III.10

Year	Actual Mortality	Cumulative Average Shipments	But-For Cumulative Average Shipments	Shipment Coefficient from Regression	Impact on Mortality	But-For Mortality	Percent Impact on Mortality
	A	*B*	*C*	*D*	*E = (B-C) * D*	*F = A - E*	*G = E / A*
2006	9.97	1.12	0.64	4.39	2.10	7.87	**21.1%**
2007	10.51	1.21	0.67	4.39	2.34	8.17	**22.3%**
2008	11.06	1.29	0.70	4.39	2.57	8.49	**23.3%**
2009	11.45	1.37	0.73	4.39	2.79	8.66	**24.4%**
2010	11.66	1.45	0.76	4.39	3.02	8.64	**25.9%**

[338] I do not extend this adjustment to Professor Cutler's analysis to the period beyond 2010, as he no longer attempts to estimate a direct relationship between opioid MMEs and prescribing during those years. He does provide a framework for extending his effect on *licit* opioids post-2010 by inexplicably assuming the relationship between cumulative average opioid MMEs and total opioid mortality can be applied to licit mortality, but that assumption is inconsistent with his own analysis that attempts to relate the reduction in opioid MMEs post-2010 to a shift from licit to illicit mortality.

Figure 50: Professor Cutler's Figure III.10, corrected to utilize prescriptions (MMEs dispensed in the retail channel)

Year	Actual Mortality	Cumulative Average *Prescriptions*	But-For Cumulative Average *Prescriptions*	*Prescription* Coefficient from Regression	Impact on Mortality	But-For Mortality	Percent Impact on Mortality
	A	*B*	*C*	*D*	*E = (B-C) * D*	*F = A - E*	*G = E / A*
2006	9.97	1.02	0.58	2.82	1.24	8.72	**12.5%**
2007	10.51	1.10	0.61	2.82	1.38	9.13	**13.2%**
2008	11.06	1.18	0.64	2.82	1.53	9.53	**13.8%**
2009	11.45	1.26	0.67	2.82	1.67	9.78	**14.6%**
2010	11.66	1.36	0.71	2.82	1.83	9.83	**15.7%**

VI.G. Plaintiffs' experts' combined damages framework is incapable of demonstrating that Allergan contributed to the alleged harm

(180) As I have described throughout this report, Plaintiffs' experts combine a long chain of unrelated national, state, and county-level estimates, measured at different points in time, and reliant on different types of measures, to reach a precise damages number for Cuyahoga and Summit counties. For example, Professor Cutler relies on several key inputs to arrive at his conclusions, as explained in the equation presented on page 12 of his expert report. The estimate of the share of opioid shipments caused by defendant misconduct comes directly from Professor Rosenthal's analysis, which is fatally flawed. The estimate of the share of opioid harms attributed to opioid shipments is based on his estimated relationship between opioid shipments and opioid mortality, which is also problematic. It is inappropriate to assume that the same relationship holds for all other types of harm, and even if it did, the estimates post-2010 are especially suspect.

(181) Plaintiffs fail to consider any measure of error and omit critical pieces of the causal chain in such a way as to invalidate any precise dollar amount they purport to measure as harm. In fact, Plaintiffs' own sensitivities show that these calculations can encompass a wide range of estimates. Professor Cutler acknowledged as much in his deposition testimony, criticizing the application of his models to a single county:

> That's why as an econometrician **you wouldn't use the analysis of this to predict for a single county**, but rather one wants to use this to develop an estimate for the set of counties as a whole because that's what this -- this is what is describing the vast --

> the average county in the data set, and that's what that regression coefficient is giving, and, therefore, it's appropriate to evaluate it at the average in the data set.[339]

Indeed, Professor Cutler testified that he would "need a different type of model entirely in order to estimate a coefficient for a single county."[340] Yet the economic framework employed by Plaintiffs' experts relies on Professor Cutler's average model precisely to do exactly that, predicting exact harm to Cuyahoga and Summit counties while offering no measure of error. In the remainder of this section, I provide additional examples of areas that Plaintiffs' experts' estimates propagate imprecision and uncertainty, the totality of which prevents them from offering a reliable estimate of harm to Cuyahoga and Summit counties.

- Both in their individual analyses and in combining their calculations, Plaintiffs' experts inappropriately multiply several different units of measurement together. For example, Professor Cutler combines his purported relationship between opioid *shipments* and mortality with Professor Rosenthal's purported relationship between manufacturer detailing and *prescription-based MMEs*. As I demonstrate in Section VI.F, substituting *prescription-based MMEs* for *shipments* (without correcting any of the other flaws in Professor Cutler's model) reduces his estimated harm by nearly half.
- Professor Cutler fails to account for differences in products when measuring harm. In his analysis, Professor Cutler assumes that the harm associated with different opioid products is all the same and that he does not need to weight his analysis in any way:

  > Q. So I'm focused on shipments that you did include in your analysis. Other than making the conversion for morphine milligram equivalents, you treated all opioid medicines as if they were the same, right?
  >
  > A. Yes. Once drugs had been converted to milligrams of morphine equivalent, and once we had decided on which drugs to include, then all drugs contributed equally, and we looked at the milligrams of morphine equivalency as a whole.[341]

  This creates two issues with his analysis. First, the assumption that the harm associated with different products is constant could be aggressive. It is conceivable that different types of opioids (both licit and illicit) contributed to harms differently. It is therefore inappropriate to assume that Allergan (which only sold particular types of branded opioids) is equally responsible for the harm associated with all types of opioid products. Second, because Professor Cutler does not take products into account in his harm calculations, it is impossible to attribute the harm to any

339 Cutler April 27 Dep. at 533:20–534:5.

340 Cutler April 27 Dep. at 529:11–13.

341 Cutler April 26 Dep. at 62:9–19 (objections omitted)

particular manufacturer, as he testified to in his deposition.[342] This flaw prevents Professor Cutler from identifying the amount of harm specific to Allergan products.

- Professor Cutler does not explain why it is appropriate to apply the percent of mortality attributable to opioids to his categories of harms. Professor Cutler claims that, "unlike crime or foster care placements, which are harms that one would expect would exist at some level even without opioids, there is no reason to expect there would be opioid-related deaths in the absence of supplies of prescription opioids and illegal substitutes."[343] However, while he claims that this idea supports the use of mortality as a clean benchmark, it is also a reason why his mortality percentages should not be applied to other metrics. For instance, the actual percentage increase for child services related to opioids may be lower than for mortality because the harm may have occurred anyway (i.e., absent opioid addiction child services may still have to deal with the same abusive parent—they just aren't using opioids). Therefore, Professor Cutler has presented no evidence that his measurements of harm "but-for" the existence of opioids are accurate, nor has he attempted to bound his estimates in any way to attempt to quantify this uncertainty.
- Professor Cutler purports to estimate the share of crime attributable to opioids by relying upon survey responses of prisoners in 2002 for an estimate of the share of each crime category that is drug-related. He applies the estimate uniformly and then uses information from the NCLIS on the share of opioids within all drugs seized and tested. Professor Cutler first assumes that the crimes surveyed would not have occurred in the absence of drugs, although the survey does not prove this assumption. Cutler also assumes that his estimate applies uniformly, although it is likely that incarceration rates, as well as drug-related crime, vary both over time and across geography. For example, in the May 2011 edition of the "National Gang Center Bulletin" published by the Bureau of Justice Assistance, U.S. Department of Justice, Howell et al. estimate that gang problems from law enforcement are highest in large cities, and the fraction of homicides linked to gang activity is very different across jurisdictions.[344] Figure 51, excerpted from the Howell et al. study, shows that gang activity in 2009 was reported in 86.2% of large cities, but only 51.8% of suburban counties, 32.9% of smaller cities, and 17.0% of rural counties. Figure 52, again excerpted from the Howell et al. study, shows that the percentage of homicides relating to gang activity varied significantly across geographic area, and the extent to which this percentage changed over time is specific to the geographic area. Figure 53 from the Howell et al. study shows significant geographic variation in the rate of gang-related homicides. As gang activity is likely to be related to the illicit opioid market, this heterogeneity of crime over time and across

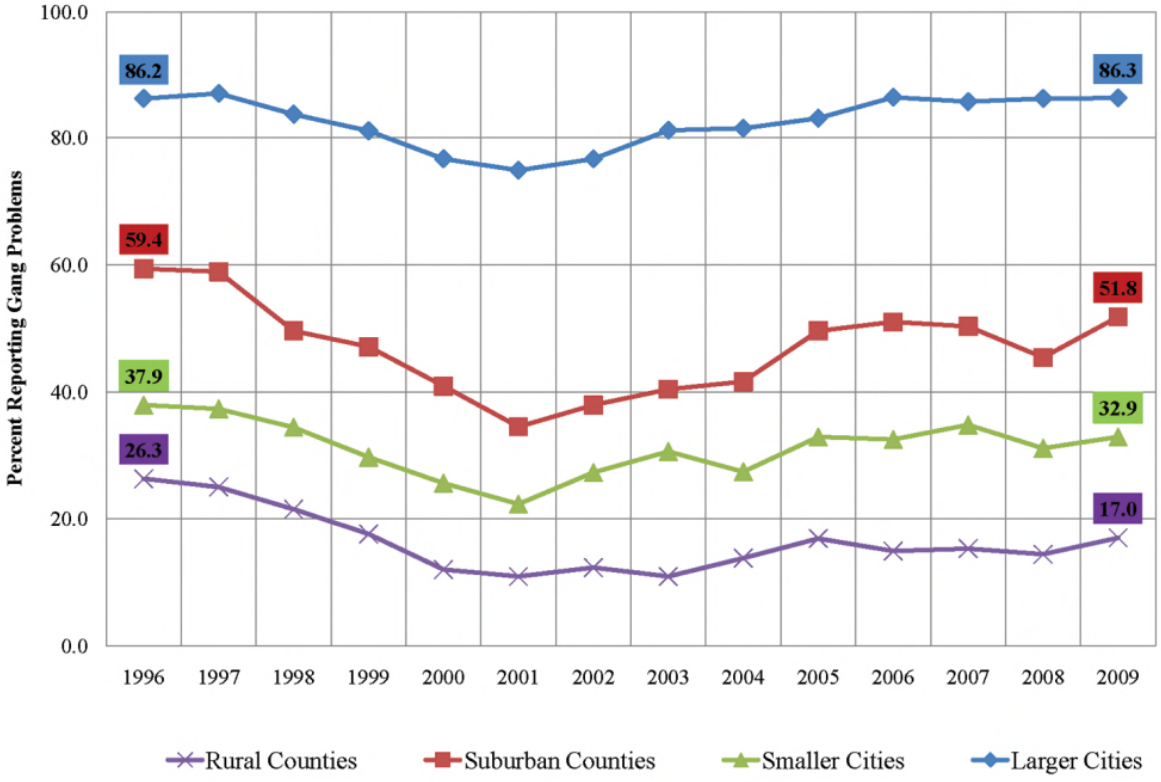
[342] "A: That's correct, I did not make any attempt to apportion harm to any individual defendant." Cutler April 26 Dep. at 55:24–55:2.

[343] Cutler Rep. ¶ 47.

[344] National Gang Center Bulletin, "U.S. Gang Problem Trends and Seriousness, 1996–2009," available at https://www.nationalgangcenter.gov/Content/Documents/Bulletin-6.PDF.

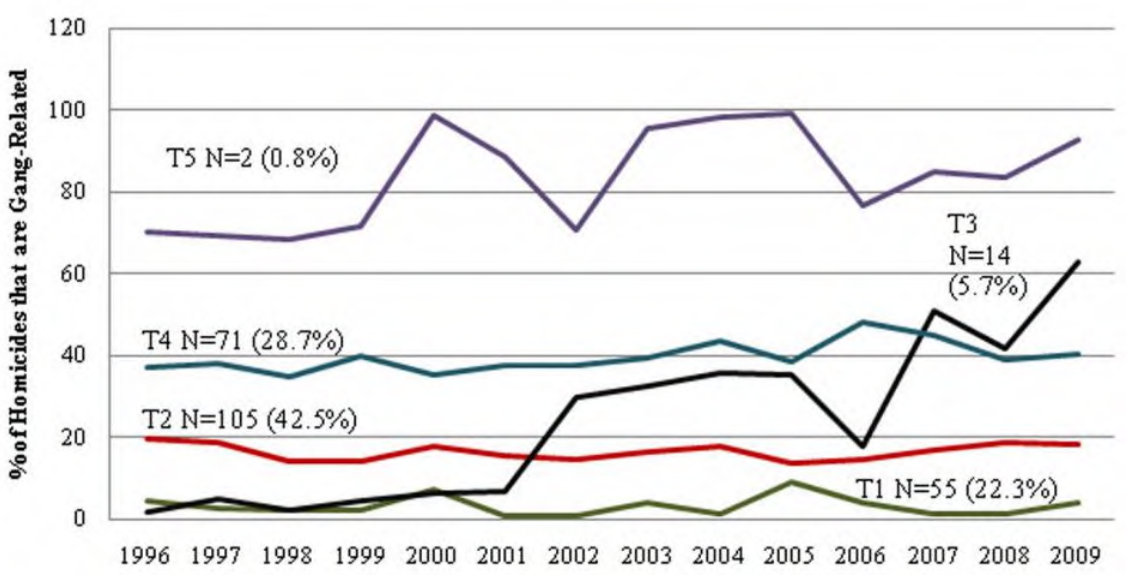
geography makes the use of a single statistic derived from national data for calculating county-specific harm very problematic.

Figure 51: Howell et al. Figure 2, "Law Enforcement Agency Reports of Gang Problems by Area Type, 1996–2009"



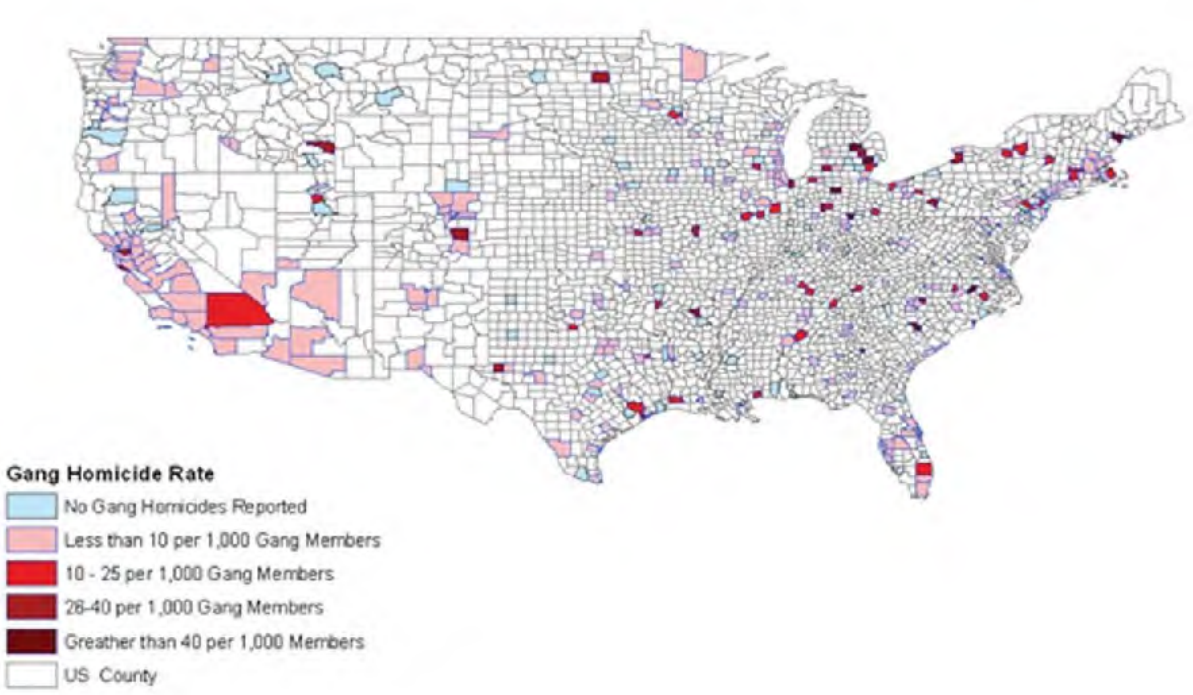
Source: Howell et al., "US Gang Problem: Trends and Seriousness," 1996-2009, Figure 2.

Figure 52: Howell et al. "Percent of Homicides That Are Gang-Related, Cities with 100,000+ population"



Source: Howell et al., "US Gang Problem: Trends and Seriousness," 1996-2009, Figure 6.

Figure 53: Howard et al. "Rate of Gang-Related Homicides (Per 1,000 Gang Members), 2002–2009"



Source: Howell et al., "US Gang Problem: Trends and Seriousness," 1996-2009, Map 2.

- Professor Cutler himself recognizes that his estimates are imprecise. In his deposition testimony, Professor Cutler admits, "there are error rates associated with any estimation,"[345] but indicates that he did not calculate them in connection with his estimation of the harm suffered by the various county departments.[346] Similarly, Professor Cutler recognizes that he has "no way to say, where the shipments in one county more of less caused by misconduct than shipments in another county," and "to the extent that they were, then there would be measurement error in the shipments variable."[347] Professor Cutler also testified that his measure of people who commit drug related crimes relies on "a proxy and so every proxy could have possible errors."[348] Despite knowing this, Professor Cutler does nothing to account for this measurement error as part of his calculations, rendering them imprecise and potentially misleading.

(182) Setting aside these issues with Professor Cutler's estimates, they are also not used properly in Professor McGuire's framework. It is not appropriate for Professor McGuire to multiply Professor Cutler's estimates of harm by a constant amount of dollars. In fact, in his deposition, Professor Cutler testified that he "show[s] the impact on events" and that "Professor McGuire's report…translates

345 Cutler April 26 Dep. at 128:14–15.

346 Cutler April 26 Dep. at 128–130.

347 Cutler April 26 Dep. at 181:22–182:4.

348 Cutler April 26 Dep. at 232:8–9.

those into dollar amounts."[349] He explains "Professor McGuire would…not be able to multiply an aggregate percentage by a total dollar amount…he would require a different input than just, for example, the percentage of that activity which is due to opioids.[350] For example, "if there were different costs for an autopsy for different reasons, that's something that Professor McGuire would need to take into account, but that's not something in this report."[351] Similarly, one might expect that a vandalism charge costs a police department significantly less than a murder charge. However, Professor McGuire applies the percent of harm calculated by Professor Cutler to total costs faced by the department, regardless of the cost of the charges related to opioid use. Indeed, Professor McGuire does exactly what Professor Cutler says he "would…not be able" to do, and merely multiplies Professor Cutler's percentage of events by his own estimates of total budgets. I discuss additional flaws in Professor McGuire's analysis in the following section.

VI.H. Professor McGuire's reports also suffer from numerous flaws

(183) An economic approach to damages requires a credible but-for (*ceteris paribus*) analysis that applies generally accepted economic methodologies to isolate the effect of the alleged harm caused by the defendant. Professor McGuire's analysis fails that test in numerous ways.

(184) Professor McGuire prepared two reports in this matter. One purports to assess economic damages to the Cuyahoga and Summit counties flowing from the alleged conduct of the Defendants, and the other to assess economic costs imposed upon the counties associated with public nuisance flowing from the Defendants' alleged misconduct. Neither of these damages estimates are calculated for specific manufacturers, and Allergan is never specifically cited by Professor McGuire. Indeed, Professor McGuire makes no effort to assess whether Allergan specifically knew of the public nuisance effects he identifies, nor to identify the consequence of Allergan's actions or inactions.

(185) As he indicates in both his damages and public nuisance reports, Professor McGuire's analysis of damages to the Cuyahoga and Summit counties is dependent on the analyses of Professor Rosenthal and Professor Cutler.[352] As I have described in detail in Sections III, IV, and VI, however, Professor Rosenthal's analysis suffers from fatal flaws that render her models incapable of assessing the impact of Defendants' promotion.

(186) Professor Cutler's analysis is also subject to severe shortcomings as I describe in Sections V and VI, failing to account for important alternative causes of the effects he estimates. His conclusions are

[349] Cutler April 26 Dep. at 192:1–3.

[350] Cutler April 26 Dep. at 194:4–10.

[351] Cutler April 26 Dep. at 193:7–12.

[352] *See* McGuire report on Damages to Bellweathers, Figure IV. 2 and the surrounding description of his methodology; Report of Professor Thomas McGuire Regarding Public Nuisance ¶¶ 46, 51, 55, 58, 61-70, fn. 72.

likewise unreliable and do not provide a credible estimate of the impact of the defendant's specific alleged conduct on the key impacts he purports to measure: crime, addiction and mental health, children's and family services, juvenile court activity, and medical examiner activity. As Professor Cutler's estimates are the root of Professor McGuire's purported damages estimates, it is critically important that Professor Cutler's estimates be measured accurately. They are not. Professor McGuire's reliance on Professors Rosenthal and Cutler therefore undermines his conclusions.

VI.H.1. Professor McGuire's economic framework is not consistent with generally accepted economic principles

(187) Professor McGuire couches his analysis in a simplistic view of local government decision making that does not give due consideration to the economic forces that impact budget determination and the expression of constituent preferences. Indeed, he says, "The analysis presented in this report is based on the view that governments allocate resources across its [sic] activities to maximize the welfare of its [sic] citizens subject to the constraints imposed by tax revenue and funds available through intergovernmental transfers."[353] Economics literature recognizes the microeconomic incentives that operate in the political process and the difficulty this presents to government officials in determining what is truly in the best interest of voters that elect them. These frictions shape government spending and budget levels as well as budget priorities.[354]

(188) The economics literature regarding the incentives that operate in political processes recognizes that government officials are constrained in their actions by the information available to them, and that the information that is available to them comes through processes that are likewise affected by the economic circumstances facing their constituents.[355] This literature recognizes that constituencies that have particularly concentrated interests are more likely to have their preferences represented in government actions than are constituencies whose interests are more diffuse or not focused on any particular issue. Ignoring the microeconomic realities of public choice can lead one to make incorrect assumptions about the constraints facing local governments and about what policies will be implemented as governments allocate resources.

(189) These microeconomic realities affect resource allocation decisions that bear a direct relationship to the assumptions Professor McGuire makes. For example, several state governments have recently decriminalized the possession of marijuana. Consequently, police officers in those states may spend less time addressing issues related to the possession of marijuana than they did previously. In essence,

353 McGuire Damages Rep. ¶ 22.

354 Professor McGuire's only clear reference to the microeconomic forces that shape government decision making is his statement that local "officials may face pressure from voters and special interests to keep taxes low even if the demand for services increases." See McGuire Damages Rep. ¶ 21.

355 An introduction to the economic theory of regulation and of collective choice is found in W. Kip Viscusi, John M. Vernon, and Joseph E. Harrington Jr, Economics of Regulation and Antitrust, 2nd edition (Lexington, MA: MIT Press, 1992) Chapter 10, 295–329.

the demand for police services has fallen as a result, or the available time police officers have had to respond to other issues has increased. A city or county facing such a reduced demand for services may face a choice between laying off officers, or finding other activities on which to spend their time and effort. The option of laying off officers would be complicated in the short run by employment rules (perhaps by union contracts, etc.) and perhaps more permanently by political opposition to reducing police presence. It is difficult for a public official to know how or where "the public" would like this newly available police resource to be allocated, and it is costly for the actual interests of the public to be clearly expressed on such an issue. Similar difficulties are present in this setting. Assuming that a fixed share of police effort is available to address opioid-abuse-related crime ignores the potential effect of other changes in the supply and demand of police effort. To simply assume that costs are proportionately assigned to opioid related crimes ignores these important confounding effects and makes the assessment unreliable.

(190) Key questions for examining the microeconomic incentives operating political processes would likely include, for example:

- Given the various issues about which voters in these counties might have cared, what would be the likely response by local government officials to changes in opioid-abuse-related activity or changes in other unaccounted for demands on the police force?
- How did key consumer segments or business groups feel about the response to these changing activities?
- What budget allocations were changed, what ballot initiatives might have been considered that reflected constituent concerns about the alleged harms? What were the outcomes of those ballot initiatives?
- What were the cause and effect of budget reductions that happened during the time in question?
- Did the counties in question, or each division within the county governments, always spend their entire budgets?
- Did any divisions seek supplemental funding to address opioid-related activity?
- How did elected officials in nearby political jurisdictions react to the opioid abuse crisis?

(191) And given all these questions, to what degree if at all did the defendant's alleged conduct contribute to the changes in constituent attitudes and the related responses by county officials? Professor McGuire does not mention these issues, let alone explore them.

VI.H.2. Professor McGuire's framework for assessing damages does not provide a reliable estimate of actual damages caused by Defendant's conduct

(192) Even if the Plaintiffs' economic experts relied upon by Professor McGuire were correct in their analysis, Professor McGuire's framework of assessing damages by evaluating his definition of opportunity cost does not provide a reliable estimate of actual damages caused by Allergan's alleged conduct, or the conduct of any of the defendants. Though Professor McGuire purports to calculate damages on the basis of "opportunity costs," he does not actually identify any opportunities that were foregone as a result of the spending he attributes to opioid-related activity. He simply assumes that any action taken to respond to opioid-related crime, for example, resulted in reduced activity that would have been directed toward some other equally valuable public bad. Professor McGuire assigns this reduction as damages. He does not test this assertion, and he explores no alternatives measures of harm.

(193) The methodology of Professor McGuire's damages report consists of three components. First, he reviews county government structures and by inspection, identifies "affected divisions" of the governments that he asserts were adversely affected by opioid abuse. Then, within each of those divisions, Professor McGuire asserts that increased services provided by the counties due to opioid-abuse led to higher costs. These he identifies as "affected costs" that include items such as activity in the county court system, the sheriff's office, and the medical examiner's office. Finally, Professor McGuire multiplies his estimates of the "affected costs" by Professor Cutler's estimated share of harms purportedly associated with manufacturers' alleged misconduct, which itself depends upon Professor Rosenthal's estimation of prescription-based MMEs purportedly attributable to manufacturers' alleged misconduct. The result of these successive multiplications is Professor McGuire's estimate of the cost consequences to the Bellwether counties of opioid-related harms purportedly attributed to manufacturer misconduct.

(194) The calculation of the shares of county division costs attributed to opioid abuse is a very rough approximation at best. In these calculations there is no identification of expenditures that actually happened as a result of opioid abuse, and certainly no identification of expenditures that occurred as a result of Allergan promotion—particularly when, as I've discussed in Section III, Allergan's shares of detailing and promotion are *de minimis*. Opioid abuse does not occur in a vacuum, and many other factors that contribute to abuse are not considered—neither by Professor McGuire nor in the estimates he uses as inputs—as I describe in Section VI.E. These include substitution effects from the use of other mind/mood altering substances such as alcohol and other drugs. Without separating the effect of opioid abuse from abuse of those other substances, Professor McGuire's analysis is incapable of attributing costs to opioid abuse.

VI.H.3. Professor McGuire inappropriately applies the concept of variable cost in his analysis

(195) Professor McGuire describes his analysis as considering the "variable costs" associated with county government expenditures. By this he refers to costs that "could move up or down as the composition of services provided" changes. For the purposes of his analysis, he refers to these costs as "affected costs" and claims that they isolate the effects of opioid abuse crisis related costs from overhead and other costs "that do not vary in response to changes in the services provided by a division."[356]

(196) While limiting the analysis of the alleged impact of opioid-abuse-related costs to variable costs is in principle the correct economic approach, Professor McGuire's methodology does not appropriately measure true variable costs. Hence, his estimate of the incremental spending by the counties attributable to manufacturers' alleged misconduct is overstated, most likely by substantial amounts.

(197) To appropriately capture the variable cost component of county expenditures that might be affected, one would need to define what costs are truly responsive to opioid harms purportedly attributed to alleged manufacturer misconduct. Consider a police officer, for example. He or she has a shift of duty during which his or her responsibilities are to respond to calls to address crime or other situations appropriate to the job. There is obviously slack in any particular police officer's (or sheriff's) schedule, as there is variation in the level of crime or related activity that the officer is called upon to address. To a large extent, any particular officer's daily activity is a fixed cost that is not necessarily affected by the type of crime he or she is addressing. An appropriate assessment of the incremental, or "affected costs" imposed upon the county's should recognize the fixed cost nature of most of the sheriff's department activities and seek evidence that the opioid abuse crisis might have contributed to truly incremental expenditures, such as changes in overtime pay or increased staffing of sheriff's deputy staff, etc. To simply assert that because another expert estimated that X% of crimes committed during a time interval were associated with opioid abuse, that a county's expenditures in responding to these crimes rose by X% is inadequate as an estimate of damages.

(198) In his analysis, Professor McGuire includes all salary expenditures for the Cuyahoga Sherriff's department as a "variable cost."[357] However, as discussed above, much of these salary expenditures would likely have occurred but for the opioid abuse crisis as police officers and sheriffs would still need to be paid their normal salaries to protect against other crimes. And even if it were the case that some portion of the normal salaries would not have occurred, Professor McGuire performs no analysis that demonstrates that *Allergan's* conduct is responsible for any of the reduced portion. This is particularly problematic considering that Allergan's promotion and prescription shares are small,

[356] McGuire Damages Report paragraph 10.

[357] McGuire AppendixIV.C_Cuyahoga_Costs, Sherriff's Office Support.

and that Plaintiffs' experts have not demonstrated that Allergan's promotion expanded prescribing, as I explain in Sections III and IV.

(199) To illustrate how sensitive Professor McGuire's analysis is to his assumptions, suppose that one were to assume as an alternative that variable costs were only those that reasonably would be avoided but for the harms purportedly quantified by Plaintiffs' economic experts. Another similarly reasonable approach would be to say that, for example, all overtime work performed by the Sheriff's department is driven by unanticipated or unplanned circumstances, such as the emergence of opioid-abuse-related crime and other problems. Applying this assumption and using the data provided by Professor McGuire, I calculate the share of all salary expenditures for the Cuyahoga County Sheriff's Department attributed to overtime pay. I find that overtime pay is only 12% of all salary expenditures.[358] Of course, this is just one example, and other analyses of the sensitivity of Professor McGuire's definition of variable costs would be appropriate. However, this illustrates the potentially substantial effect of differing reasonable definitions of this important concept.

(200) Also, Professor McGuire's determinations of affected costs and their variable components rely on imprecise information that is difficult to verify or validate, such as phone conversations between members of his team at Compass Lexecon with unidentified employees of Cuyahoga and Summit counties.

VI.H.4. Professor McGuire's analysis of "Public Nuisance" suffers from many of the same flaws as his "damages" analysis

(201) Professor McGuire's analysis of the impact of opioid abuse on the effect of "Public Nuisance" suffers from many of the same problems as discussed above. As with his damages report, his assessment of public nuisance depends critically on the reports of Professor Cutler and Professor Rosenthal.[359] As I discuss above, the serious flaws in those reports render Professor McGuire's conclusions unreliable. This, in combination with the shortcoming in Professor McGuire's economic framework and methods, render his conclusions unreliable as an estimate of public nuisance attributable to Allergan. In both this report and the report on damages, Professor McGuire does not meaningfully distinguish between harm from opioid abuse and harms from opioid sales overall. He offers no clear justification

[358] I calculated the overtime expenditure for the Cuyahoga Sheriff's department using Professor McGuire's Cuyahoga expenditure data (CUYAH_014627783). Using these data, I determined the number of regular hours and the number of overtime hours worked by the employees in the Sheriff's department divisions that were identified by Professor McGuire. I then calculate the share of salary expenditure associated with overtime hours under the assumption that employees are paid one and a half times their normal pay rate for any overtime hours. *See* Cuyahoga County & Ohio Patrolmen's Benevolent Association "Deputy Sheriffs' Contract," available at http://legal.cuyahogacounty.us/pdf_legal/en-US/CollectBarg/DeputySheriffsContract.pdf.

[359] Professor McGuire relies upon Professor Rosenthal's "under-treated pain" analysis to assess "whether the shipments were reasonable" and on Professor Cutler's "Approach 1" to "determine the absolute numbers of deaths each year attributable to shipments" and on other "opioid-related harms" McGuire public nuisance report, ¶¶ 46, 51, 55, 58, 61-70, fn. 72

for the assumption that all excess shipments are due to alleged defendant misconduct. He does not establish a reasonable degree of a causal relationship between opioid abuse and the set of ills he discusses, much less tie them to the alleged actions of Allergan. In fact, despite claiming to measure the "harms due to defendants' shipments," Professor McGuire specifically states that his measures of harm include harm that Professors Rosenthal and Cutler have measured as *unrelated* to the alleged misconduct.[360]

> Professor Cutler estimated the share of studied harms due to Defendants' misconduct by multiplying Professor Rosenthal's estimated share of shipments due to misconduct by his own estimate of the share of harms due to shipments. **In this Report, I assess the external costs associated with prescription shipments without regard as to whether they were due to Defendants' misconduct**. I thus use the share of harms due to shipments without multiplying by Professor Rosenthal's estimate of the share of shipments due to misconduct.[361]

(202) As a specific example of the methodological problems afflicting Professor McGuire's report, his methodology does not account for omitted alternative explanatory factors, many of which I describe in Section VI.E, and as such leaves room for substantial uncertainty and error in his results. Specifically, the externalities that Professor McGuire identifies as associated with opioid abuse are not identified distinctly from those associated with other addictive (or mood and behavior altering) substances such as alcohol. It is very plausible that many of the social costs that the Plaintiffs assert are related to opioids would have occurred even without opioids: for example, literature suggests that opioid addiction is more likely in individuals with a history of addiction to other substances. [362] Professor McGuire clearly understands the negative social consequences of alcohol use but he does not explore this important interaction.[363]

(203) From the perspective of basic economic theory, without establishing, or even considering the degree to which use of opioids and alcohol, cocaine, and other substances are related to opioids, one cannot reliably assess to what degree any one of these products is responsible for various social ills. All might have contributed absent the contribution of another, so failing to consider such possibilities

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360 McGuire public nuisance report, fn. 57, Table 1

361 McGuire public nuisance report, fn. 57

362 *See e.g.*, Lynn R. Webster and Rebecca M. Webster, "Predicting Aberrant Behaviors in Opioid-Treated Patients: Preliminary Validation of the Opioid Risk Tool," Pain Medicine 6, no. 6 (2006), 432–442;

Philippe Lucas et al. "Medical cannabis patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances," Harm Reduction Journal 16, no. 9 (2019), 1–11;

Yih-Ing Hser, M. Douglas Anglin, and Keiko Powers, "Longitudinal patterns of alcohol use by narcotics addicts," Recent Developments in Alcoholism: an Official Publication of the American Medical Society on Alcoholism, the Research Society on Alcoholism, and the National Council on Alcoholism 8, (1990), 145–171.

Paul Cushman, Jr. (1987) Alcohol and Opioids: Possible Interactions of Clinical Importance, *Advances in Alcohol & Substance Abuse*, 6:3, 33–46.

363 *See* McGuire Nuisance Rep. ¶27.

does not yield an appropriate *ceteris paribus* estimate of public nuisance. This fact alone casts serious doubt on the exercise Professor McGuire undertakes in this report.

(204) In addition, I see no attempt by Professor McGuire to assess the calculated causal effects of marketing behavior he adopts from Professor Rosenthal in light of other potential drivers of opioid abuse. As discussed in Section VI.E, Case and Deaton[364] identify psychological stress and other sources of "despair" as important contributors to suicide, accidental poisonings and opioid-related harms. It is certainly reasonable to consider the possibility that trends and reductions in opportunities contributed to the opioid abuse crisis, and, perhaps directly to other ills that Professor McGuire associates with opioid use, such as child mistreatment and crime.

(205) As he considers the potential offsetting benefits from opioid use, Professor McGuire, as do other plaintiff experts, takes a very narrow view of appropriate use of prescription opioids and he makes almost no effort to consider potential patient benefits beyond a very narrow range. He also discounts the benefits that patients on opioid therapy received from such therapy if he deems it "inappropriate." Obviously, those patients—the overwhelming majority of whom do not misuse opioids—would not continue utilizing a treatment that provided them no benefit. Ignoring that benefit results in a bias in Professor McGuire's analysis. Furthermore, in describing the conditions for which these products are appropriately used, he appears to offer clear medical opinions about appropriate use. He writes:

> Chronic opioid therapy is not recommended for most common chronic pain conditions, including low back pain, centralized pain such as fibromyalgia, and headache pain. In less common chronic pain conditions (such as pain from advanced multiple sclerosis, sickle cell disease, pain following spinal cord injury and paraplegia, or post-herpetic neuralgia), which comprise a small percentage of chronic pain patients, opioids may be considered a third-line therapy (taken if other therapies are ineffective or contraindicated) for moderate and severe pain. However, in other neurologic conditions such as polyneuropathy, no functional status markers were improved by long-term use of opioids, adverse outcomes were more common among patients with polyneuropathy receiving long-term opioids, including depression, opioid dependence and opioid overdose. In addition to diagnosis, clinicians should consider risk, and some patients may not be suitable candidates on the basis of that risk. Given the narrow categories that may indicate opioids for chronic use, opioids' position as third-line therapy, and the significant risks associated with its use, long-term opioid therapy for persons with chronic conditions is, at most, indicated in fewer than 5% of patients with chronic pain and likely significantly fewer. For all proper indications other than terminal cancer, palliative care and hospice care, if prescribed,

[364] *See* Anne Case and Angus Deaton, "Mortality and morbidity in the 21st century," *Brookings Papers on Economic Activity*, (2017), 397–476.

> opioids should be prescribed with the lowest effective does of immediate-release opioids taken only when needed."

(206) Although I do not offer a medical opinion about what is or is not an appropriate use of prescription opioids or any other medicine, I note that Professor McGuire's (and Professor Rosenthal's) extremely limited view of appropriate use is at odds with several other authoritative sources, including the FDA and prescribing guidelines. The FDA approved label for Kadian, for example, indicates that it was not recommended for immediate post-operative pain, but it was recommended for use when pain relief was needed over an extended period. Applying the criteria adopted by Professors McGuire and Rosenthal implies that the FDA erred either in its approval of Kadian for long-term use, or its labelling as such. Professor McGuire also does not acknowledge that appropriate medical use, across all classes medications, is ultimately determined by the treating physician. The assertion that any prescription of opioids is medically inappropriate if it exceeds the narrow definitions identified by Professors McGuire and Rosenthal is not justified. Physicians evaluate any particular patient's need and to determine a course of treatment that is most appropriate for the patient given that patient's particular circumstance. As I discuss in Section VI.D, I understand that Dr. Warfield indicates that such physician judgment leads to opioid use for conditions and in dosages outside of the narrow ranges suggested by Professors Rosenthal and McGuire.

(207) The opinion that the vast majority of prescription opioids are inappropriately used is also at odds with published research that indicates that in 2015, only 4.7% of users of prescribed opioids misused them, only 0.8% had a misuse disorder, and of those misusing prescription opioids, 60% did not have a prescription.[365] Using methods similar to those of Professor McGuire, these results would suggest that *all* promotion might be responsible for just under 1.9% (40% of 4.7%) prescription opioid misuse. Allergan has only a tiny share of promotion, implying that its share of this 1.9% is essentially zero. Moreover, similar methods with other evidence suggests that of this small number, we could expect fewer than 4% to begin using heroin within five years.[366]

(208) Finally, Professor McGuire fails to account for the fact that not all opioids are equally likely to be abused. There is good evidence, for example, that morphine is less prone to abuse than are other opioids.[367] Hence, the likelihood of adverse events being caused by prescribed morphine products is lower than it would be for other opioid products. Consequently, Professor McGuire's approach causes him to overstate the share of damages linked to products such as Kadian, a form of morphine.

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[365] *See* Han et al., "Prescription Use, Misuse, and Use Disorders in US Adults," *Annals of Internal Medicine* 167, no. 5 (2017), 293–302

[366] Pradip K. Muhuri et al., "Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States," CBHSQ Data Review, Substance Abuse and Mental Health Services Administration available at http://www.thblack.com/links/rsd/SAMHSA_Aug2013_HeroinUse.pdf

[367] *See* Wightman et al., "Likeability and Abuse Liability of Commonly Prescribed Opioids," *Journal of Medical Toxicology* 8 (2012), 335–340.

May 10, 2019

Margaret K. Kyle, PhD

Date

Appendix A. Curriculum vitae of Margaret K. Kyle, PhD

A.1. Education

- Ph.D. Economics, Massachusetts Institute of Technology, 2002.
- B.S. with honors, Cornell University, 1995.

A.2. Teaching and research fields

- Industrial Organization, Productivity, Economics of Innovation, Health Policy, Business Strategy

A.3. Work experience

- Professeur, MINES ParisTech, 2014- (Chair in Intellectual Property and Markets for Technology, 2016-).
- Visiting Professor, Northwestern University (Kellogg School), 2014-.
- Professeur, Université de Toulouse 1 and Toulouse School of Economics, 2010–2014.
- Visiting Professor, University of Hong Kong, 2013.
- Professeur associé, Université Toulouse 1 and Toulouse School of Economics, 2009–2010.
- Assistant Professor, London Business School, 2006–2010 (on leave 2009–10).
- Assistant Professor, Duke University, Fuqua School of Business, 2004–2006.
- Assistant Professor, Carnegie Mellon University, Tepper School of Business, 2002–2004.
- Visiting Scholar, Center for the Study of Innovation and Productivity, Federal Reserve Bank of San Francisco, 2003.
- Research Assistant, Board of Governors of the Federal Reserve System, 1995–1997.

A.4. Research

A.4.a. Publications in refereed journals

- "Deregulating Direct-to-consumer Marketing of Prescription Drugs: Effects on Prescription and Over-the-counter Sales," with Ernst R. Berndt and Davina Ling (2002), *Journal of Law and Economics* 44 (3), 691–723.
- "Measuring health impacts on work performance: Comparing subjective and objective reports," with Glenn Pransky, Ernst Berndt, Stan Finkelstein, Joan Mackell, and Dan Tortorice (2002), *Value in Health* 5(6), 448–449.
- "Public & Private Spillovers, Location, and the Productivity of Pharmaceutical Research," with Jeff Furman, Iain Cockburn, and Rebecca Henderson, *Annales d'Economie et Statistique* 2005, 79/80, 165–188.
- "Surviving the Gales of Creative Destruction: The Determinants of Product Turnover," with John M. de Figueiredo (2006), *Strategic Management Journal* 27(3), 241–264.
- "Objective and Self-Reported Work Performance Measures: A Comparative Analysis," with Glenn Pransky, Ernst Berndt, Stan Finkelstein, Joan Mackell, and Dan Tortorice (2006), *International Journal of Productivity & Performance Management* 55(5), 390–399.
- "The Role of Firm Characteristics in Pharmaceutical Product Launches," *RAND Journal of Economics* Autumn 2006, 37(3), 602–618.
- "Pharmaceutical Price Controls and Entry Strategies," *Review of Economics and Statistics* February 2007, 89(1), 88–99.
- "Generic Competition and Market Exclusivity Periods in Pharmaceuticals" (2007) with Henry Grabowski, *Managerial and Decision Economics* 28(4–5), 491–502.
- "Would Greater Price Transparency and Uniformity Benefit Poor Patients?" with David Ridley, *Health Affairs* Sept/Oct 2007, 26(5), 1384–1391.
- "Does Re-importation Reduce Price Differences for Prescription Drugs? Lessons from the European Union," with Jennifer Allsbrook and Kevin Schulman, *Health Services Research* August 2008, 43(4), 1308–1324.
- "Intervening in global markets to improve access to HIV/AIDS treatment: an analysis of international policies and the dynamics of global antiretroviral medicines markets" (with Brenda Waning, Ellen Diedrichsen, Lyne Soucy, Jenny Hochstadt, Till Barnighausen and Suerie Moon), *Globalization and Health* 2010, 6:9.
- "Strategic Responses to Parallel Trade" (2011), *The B.E. Journal of Economic Analysis & Policy*: Vol. 11: Iss. 2 (Advances), Article 2.
- "Assessing the population health impact of market interventions to improve access to antiretroviral treatment," with Till Barnighausen, Joshua Salomon and Brenda Waning, September 2011, *Health Policy and Planning*, doi: 10.1093/heapol/czr058.

- "Evolving Brand-Name And Generic Drug Competition May Warrant A Revision Of The Hatch-Waxman Act," with Henry Grabowski, Richard Mortimer, Genia Long and Noam Kirson, November 2011, *Health Affairs* 30:2157–2166.
- "Investments in Pharmaceuticals Before and After TRIPS" (2012), with Anita McGahan, *Review of Economics and Statistics*, 94(4): 1157–1172.
- "Intellectual Property Protection and the Geography of Trade" (2013), with Mercedes Delgado and Anita McGahan, *Journal of Industrial Economics* 61(3): 733–762.
- "Competition and the Efficiency of Markets for Technology" (2015), with Marie-Laure Allain and Emeric Henry, *Management Science*, 62(4):1000–1019.
- "Competition Law, Intellectual Property, and the Pharmaceutical Sector" (2016), *Antitrust Law Journal*, 81(1):1–45.
- "Is American Health Care Uniquely Inefficient? Evidence from Prescription Drugs" (2017), with Heidi L. Williams, *American Economic Review Papers & Proceedings*, 107(5):486–490.
- "Strategic Interaction among Governments in the Provision of a Global Public Good" (2017), with David Ridley and Su Zhang, *Journal of Public Economics*, 156: 185–199.
- "Are Important Innovations Rewarded? Evidence from Pharmaceutical Markets" (2018*), Review of Industrial Organization*, 53(1):211–234.
- "The More We Die, The More We Sell? A Simple Test of the Home-Market Effect" (with Arnaud Costinot, Dave Donaldson, and Heidi Williams), *Quarterly Journal of Economics*, forthcoming.
- "The Single Market in Pharmaceuticals," *Review of Industrial Organization*, forthcoming.

A.4.b. Book chapters and other publications

- "Did U.S. Bank Supervisors Get Tougher During the Credit Crunch? Did it Matter to Bank Lending?" with Allen N. Berger and Joseph M. Scalise in *Prudential Supervision: What Works and What Doesn't*, edited by Frederic Mishkin (Chicago: University of Chicago Press, 2001).
- "The Long Shadow of Patent Expiration: Do Rx to OTC Switches Provide an Afterlife?" with Ernst R. Berndt and Davina Ling, *in NBER Conference Volume on Scanner Data and Price Indexes*, edited by Robert Feenstra and Matthew Shapiro (Chicago: University of Chicago Press, 2003), 229–267.
- "Does Locale Affect R&D Activity? The Case of Pharmaceuticals," *Federal Reserve Bank of San Francisco Economic Letter*, Nov. 13, 2004.
- "Product Launch Decisions by Dominant and Fringe Firms," with John M. de Figueiredo, *Best Paper Proceedings of the Academy of Management*, 2005.

- "Mergers and Alliances in Pharmaceuticals: Effects on Innovation and R&D Productivity," with Henry Grabowski, in *The Economics of Corporate Governance and Mergers*, edited by Klaus Peter Gugler and B. Burcin Yurtoglu (Cheltenham, UK: Edward Elgar Publishing, 2008).
- "Innovation in the Pharmaceutical Industry," report prepared for the National Endowment for Science, Technology and the Arts, May 2008.
- "Comparative advantages of push and pull incentives for technology development: lessons for neglected diseases" with Cheri Grace, in *Global Forum Update on Research for Health Volume 6*, 2009.
- "Parallel Trade in Pharmaceuticals: Firm Responses and Competition Policy," Chapter 13 in *International Antitrust Law & Policy: Fordham Competition Law 2009*, edited by Barry Hawk (Juris Publishing, New York, 2009).
- "Consolidation and Productivity in the Pharmaceutical Industry," with Henry Grabowski, in P. Danzon and S. Nicholson, editors, *Handbook of the Economics of the BioPharmaceutical Industry* (Oxford, 2012).
- "Markets for Pharmaceutical Products," with Fiona Scott Morton, Chapter 12 in M.V. Pauly, T.G. McGuire, and P.P. Barros, editors, *Handbook of Health Economics Volume 2* (Elsevier, 2012), pp. 763–823.
- "Alliances, Mergers and Acquisitions," with Henry Grabowski, in Anthony J. Culyer, editor, *Elsevier Encyclopedia of Health Economics* (Elsevier, 2013).
- "US healthcare inefficiency: Evidence from international prescription drug data," VoxEU 22 May 2017 (with Heidi Williams).
- "When a government increases funding for research on a disease, others spend less," VoxEU 14 December 2017 (with David Ridley and Su Zhang).
- "Forward: e-Competitions Special Issue on Competition in the Pharmaceutical Sector," *e-Competitions Bulletin*, Article 88600, 13 December 2018.
- "Trade in IP-Intensive Goods" (2019), forthcoming in *Trade in Knowledge* (with Mercedes Delgado).

A.4.c. Working papers

- "Strategic Responses to Cultural Quotas: Evidence from French Radio" (with Dandan Niu)
- "Estimating the Effects on Mortality Rates of Cancer Drug Innovation" (with Pierre Dubois)
- "Experts and Financial Ties: Evidence from FDA Advisory Committees," with Fanny Camara.
- "Intellectual Property Rights and Access to Innovation: Evidence from TRIPS," with Yi Qian.

A.4.d. Work in progress

- "Entry Agreements and Generic Competition," with Annabelle Marxen.
- "Globalization and Innovation: Theory and Evidence from the Pharmaceutical Industry" (with Arnaud Costinot, Dave Donaldson, and Heidi Williams)
- "Music Streaming and Royalty Payments"
- "The Evolution of the Market for HIV Treatments," with Pai (Steven) Xu.
- "Intellectual Property Rights and Cumulative Innovation," with Nina Yin.

A.4.e. Invited talks

- 2001–2002: Boston University School of Management; UC-Irvine Graduate School of Management; Carnegie Mellon University GSIA; Washington University in St. Louis, Olin School of Business; University of Michigan, Ford School of Public Policy; U.S. Department of Justice; UC-Davis Department of Economics; Federal Reserve Bank of San Francisco; Board of Governors of the Federal Reserve System; University of Toronto Rotman School of Management; London Business School; University of Washington, School of Business; NBER Productivity Lunch; NBER Summer Institute.
- 2002–2003: Duke University Fuqua School of Business; Stanford Strategic Management Conference; International Health Economics Conference; NBER-CREST Joint Conference on R&D, Education, and Productivity.
- 2003–2004: Federal Reserve Bank of San Francisco; Wharton Technology Conference; Northwestern University Kellogg Graduate School of Management; International Schumpeter Society Conference; Southern Economics Association Conference; International Health Economics Association Conference.
- 2004–2005: NBER Productivity Lunch; Duke University Department of Economics; University of Miami; Cornell University.
- 2005–2006: Lehigh University; University of Toulouse; London Business School; HEC Lausanne; London School of Economics; Imperial College; New York University; NBER Summer Institute.
- 2006–2007: OECD Committee for Science and Technological Policy meeting; DRUID Winter Conference; Strategy Research Forum; International Health Economics Association Conference; NBER Pre-conference on Location of Biopharmaceutical Activity.
- 2007–2008: University of Basel; University of St. Andrews; Paris School of Economics; NBER Productivity Lunch; NBER Conference on the Location of Biopharmaceutical Activity; Duke

Strategy Conference; MIT Business and Public Policy Conference; American Society of Health Economists Conference; Knowledge for Growth Conference; NBER Summer Institute.

- 2008–2009: Markets for Technology Conference; London Business School; Wharton; University of Missouri; Harvard Business School; INSEAD; Emory University; NBER Productivity Lunch; Duke University Fuqua School; HEC Lausanne; Free University of Brussels; University of Toulouse; Imperial College; Network of Industrial Economists Conference.
- 2009–2010: Fordham Conference on International Antitrust Law and Policy; European School of Management and Technology; Wharton Conference on the Pharmaceutical Industry; University of Tokyo; University of Zurich; Korea-US Healthcare Innovation Seminar.
- 2010–2011: Toulouse School of Economics (IO and IP workshops); Pharmaceutical Economics and Policy Council conference; University of Basel; CSIO-IDEI conference.
- 2011–2012: EARIE conference; Triangle Health Economics seminar; Toulouse School of Economics; University of Zurich; University of Hong Kong; USPTO Conference on Patents, Entrepreneurship and Innovation.
- 2012–2013: Duke; Georgetown; University of Hong Kong; Tsinghua University; Peking University; Copenhagen Business School; Northwestern Research Roundtable on Technology Standards, Innovation, and Market Coordination; Toulouse IP Conference; World Intellectual Property Organization; NBER Summer Institute; Academy of Management Conference.
- 2013–14: KU Leuven; University of Mannheim; CERGE-EI; Symposium on European Competition Law; MINES ParisTech; University of East Anglia (Economics Department and the Centre for Competition Policy); Toulouse Health Economics Conference; Kellogg; BatesWhite Healthcare Symposium; University of Michigan.
- 2014–15: EARIE conference; OECD-JPO Conference on Patent Statistics; DIW Berlin; ASSA meetings; Paris School of Economics.
- 2015–16: DRUID; Journée de la Chaire Santé; IIOC; HEC; Auctions, Competition, Regulation and Public Policy Conference; ASHEcon; EUHEA
- 2016–17: EARIE conference; Queen's University; CREST; ASSA meetings; World Trade Organization; Penn Law School; University of Michigan; BatesWhite Healthcare Symposium; IIOC; University of Lausanne; CCP Conference on Competition Issues in Pharmaceuticals; International Health Economics Association Conference.
- 2017–18: EARIE Conference; EPIP conference; CREST-ECODEC Conference on the Economics of Antitrust and Consumer Protection; Tilburg; Max Planck; Conference on Economic Developments in Competition Policy, Brussels; Second Medical Use Conference, Washington; Seminar on health innovation, Berne; Innovation Economics for Antitrust Lawyers Conference, London; Case

- Western Reserve University; WHO/WTO/WIPO Trilateral Symposium, Geneva; Celebrating 25 Years of the EU Single Market, Cambridge, UK; IPRs and Human rights: Economic and policy challenges, Pisa; ETH Zurich.
- 2018–19 (planned): EPIP conference; WTO; OECD Competition Committee; NBER Innovation Policy and the Economy conference; Rethinking Trade Treaties & Access to Medicines conference; DG Competition; Bates White Life Sciences Symposium.

A.5. Teaching

- *MINES ParisTech*
  - Cycle d'économie pour les ingenieurs des mines
  - Technology and Innovation Strategy
  - Co-director, option in Industrial Economics
- *Toulouse School of Economics/University of Toulouse 1*
  - Director of the "Management of Innovation" degree (M2)
  - Innovation Strategy (M2) 2012–2014.
  - Quantitative Data Analysis (M1), 2012–2014.
  - Business Strategy (M2), 2009–2012.
  - Protocole de recherche (M2), 2010.
  - Advanced Strategy (M1), 2009–2011.
- *Northwestern University, Kellogg School of Management*
  - Pharmaceutical Strategy (MBA elective), 2015, 2017, 2018.
  - Technology and Innovation Strategy (MBA elective), 2014.
- *University of Lausanne, Swiss School of Public Health*
  - The Industrial Organization of the Pharmaceutical Industry (PhD), 2013.
- *University of Basel, Zaeslin Program in Law and Economics*
  - Competition and Regulation in the Pharmaceutical Industry (M1), 2009–12.
- *London Business School*
  - Economics of Competitive Strategy (MBA elective), Fall 2006, Spring 2008.
  - Strategy in Innovative Industries (MBA elective), Fall 2008.

- Core Strategy (EMBA programs), Spring and Summer 2007, Spring 2008.

- *Duke University, Fuqua School of Business*
  - Pharmaceutical Economics and Management (co-instructor, Fall 2011, Fall 2012).
  - Core Strategy (EMBA programs), Fall 2004, Fall 2005, Spring 2006.
  - Management of Innovation and Technology (MBA elective), Fall 2005, Spring 2005.
- *Carnegie Mellon University, Tepper School of Business*
  - Technology Strategy (MBA elective). Spring 2003 (2 sections), Spring 2004 (4 sections)
  - Technology Strategy (undergraduate elective). Spring 2003
  - Economics of Innovation (PhD course). Spring 2004

A.6. Professional activities

- Public service
  - Member of the Conseil National de Productivité, France.
- Grants and research contracts
  - Agence Nationale de la Recherche, "Economics of Antibiotics: Incentives for Innovation and Implications for Health Care Costs" (with Pierre Dubois)
  - World Bank, effects of TPP on pharmaceutical markets in Thailand
  - European Commission, for an economic report on the functioning of Supplementary Protection Certificates (SPC) in Europe
  - Chaire Sant´e, "The Evolution of the Market for Antiretroviral Treatments in Developing Countries"
  - Chaire Sant´e, "Government Funding of Medical Research"
  - Department for International Development (UK), for "Survey on Pharmaceutical Product Division from Low-income to High/Middle-income Settings"
  - Pfizer, for "Cancer Treatments and Survival: Evidence from Europe and the US" (with Pierre Dubois)
  - World Health Organization, for "Establishment and Maintenance of a Global Public Good, the Global Data Exchange for Market Intelligence"
  - UNITAID, for "Framework to Monitor Markets and Assess the Market Impact of UNITAID's Interventions in Low-resource Settings"

- PhRMA, for "Research and Development Incentives for Neglected Diseases" (with David Ridley)
- Pfizer, for "Innovation in Vaccines" (with David Ridley)
- National Endowment for Science, Technology and the Arts (NESTA), for "Innovation in the Pharmaceutical Industry"

- Editing and Refereeing
  - Associate editor, International Journal of Industrial Organization
  - Referee for *American Economic Review, Econometrica, Journal of Political Economy, Quarterly Journal of Economics, Review of Economic Studies, Management Science, Review of Economics and Statistics, Journal of the European Economic Association, RAND Journal of Economics, Journal of Industrial Economics, Journal of Economics and Management Strategy, International Economic Review, European Economic Review, Research Policy, Journal of Development Economics, Journal of Law and Economics, Journal of Economic Analysis and Policy, Economic Inquiry, Economic Journal, Health Affairs, Health Economics, International Journal of Health Care Finance and Economics, Journal of Health Economics, Journal of Public Economics, Economics of Innovation and New Technology, Economic Inquiry, Economic Letters, Southern Economic Journal, Journal of Regulatory Economics, Journal of Applied Econometrics, Journal of Economic and Business Statistics, Scandinavian Journal of Economics, Journal of Banking and Finance, Journal of Money, Credit and Banking, Review of Industrial Organization, Social Science and Medicine, Global Public Health, Globalization and Health, Academy of Management Journal, Strategic Management Journal*, US National Science Foundation, UK Economic and Social Research Council, Netherlands Organisation for Scientific Research, Swiss National Science Foundation.
- Conference organization
  - Co-organizer (with Philippe Aghion) of conference on trade and innovation, 2017.
  - Member of the scientific committee for the EARIE Conference, 2017, 2018, 2019.
  - Member of the scientific committee for the CEPR Industrial Organization Conference, 2011–2015.
  - Co-organizer (with Pierre Dubois) of the Toulouse TIGER conference on health economics, 2014.
- Professional Memberships
  - Research Fellow (Industrial Organization), Centre for Economic Policy Research
  - American Economic Association

- European Association for Research in Industrial Economics
- Industrial Organization Society
- American Society of Health Economics

Appendix B. Materials considered

I incorporate by reference all materials cited in my expert report.

B.1. Data

- 7.5_Standardized_prices_of_cocaine_and_heroin_in_the_United_States_and_Western_Europe.xlsx.
- ALLERGAN_MDL_01890663.xlsx (Kadian call notes)
- Analysource Data File.xlsx
- BOP_MDL 5th Production 000001—000044 (Ohio Automated Rx Reporting System (OARRS) data)
- CD light zip code crosswalk (ziplist5.txt)
- Cutler backup data.
- CUYAH_014627783.xls (Cuyahoga expenditure data)
- DEA ARCOS NDC Dictionary
- FDA NDC directory (package.txt and product.txt)
- IQVIA Xponent and PlanTrak data
- McCann backup data.
- McGuire backup data.
- NASA sunspot data (SN_m_tot_V2.0.txt)
- Rosenthal backup data.
- SNL Kagan zip code to county list.xlsx
- USPS Quarter 2014 Zip-County Crosswalk (ZIP_COUNTY_122014.xlsx)

B.2. Depositions and exhibits

- Deposition of Jennifer Altier, August 2, 2018.
- Deposition of Julie Snyder, November 2, 2018.

- Deposition of Douglas Boothe, January 17, 2019.
- Deposition of Nathalie Leitch, January 22, 2019.
- Deposition of Matthew Perri, III, BS Pharm, Ph.D., Rph, April 23, 2019.
- Deposition of Thomas G. McGuire, Ph.D., April 23, 2019.
- Deposition of Matthew Perri, III, BS Pharm, Ph.D., Rph, April 24, 2019.
- Deposition of Jonathan Gruber, Ph.D., April 25, 2019.
- Deposition of David Cutler, Ph.D., April 26, 2019.
- Deposition of David Cutler, Ph.D., April 27, 2019.
- Deposition of Thomas G. McGuire, Ph.D., April 30, 2019.
- Deposition of Meredith B. Rosenthal, Ph.D., May 4, 2019.
- Deposition of Meredith B. Rosenthal, Ph.D., May 5, 2019.

B.3. Discovery

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- Expert Report of David Kessler, MD., March 26, 2019.
- Expert Report of Dr. Jeffrey B. Liebman, March 25 2019.
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- Expert Report of G. Caleb Alexander, MD, MS, March 24, 2019.
- Expert Report of Katherine Keyes, March 24, 2019.
- Expert Report of Mark A. Schumacher, MD, Ph.D., March 25, 2019.
- Expert Report of Matthew Perri III, BS Pharm, PhD, RPh., March 25, 2019.
- Expert Report of Professor David Cutler, March 25, 2019.
- Expert Report of Professor Jonathan Gruber, March 25, 2019.
- Expert Report of Professor Meredith Rosenthal, March 25, 2019.
- Expert Report of Theodore Parran, March 25, 2019.
- Expert Report of Thomas McGuire Damages to Bellwethers, March 25, 2019.
- Expert Report of Thomas McGuire Regarding Public Nuisance, March 25, 2019.
- Second Supplemental Expert Report of Craig J. McCann, Ph.D., CFA, April 15, 2019.
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- Expert Report of Lacey R. Keller, April 15, 2019.

B.5. Filings

B.5.a. Case law, expert, litigation, and legislation

- Allergan Finance, LLC's Objections and Responses to Plaintiffs' Corrected Second Set of Interrogatories. *In re National Prescription Opiate Litigation*. MDL No. 2804. Case No. 17-md-2804 (N.D.Ohio August 31, 2018.) pp. 1–44.
- Allergan's Fourth Amended Objections and Responses to Plaintiffs' Corrected Second Set of Interrogatories. *In re National Prescription Opiate Litigation*. MDL No. 2804. Case No. 17-md-2804 (N.D.Ohio Mar. 4, 2019.) pp. 1–60.
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- Declaration of Meredith Rosenthal in Response to Defendants' Expert Keith E. Argenbright. M.D. *In re Neurontin Marketing, Sales Practices, and Products Liability Litigation*. MDL Docket No. 1629. Master File No. 04-10981. (D.Ma. September 14, 2006) ¶ 1–20.
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- Memorandum of Decision Dismissing Cases for Lack of Jurisdiction, *New Haven v. Purdue Pharma*, No. CV-17-6086134-S, Dkt. 244, (Conn. Super. Ct. Jan. 8, 2019): pp. 1–16.
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Appendix C. Summary of Plaintiffs' economic expert opinions

(209) As described in Section I.D, Plaintiffs' experts purport to estimate the harm suffered by the Bellwether counties caused by opioid shipments that resulted from defendants' misconduct. This appendix outlines those opinions in more detail.

C.1. Professor Rosenthal's estimation of the percentage of shipment-related harms that is attributable to defendants' misconduct

(210) Professor Rosenthal was asked by counsel for Plaintiffs to determine the "[e]xtent of 'but for' causation," among other charges. Specifically, Professor Rosenthal was asked whether she has "an opinion as to the quantum of increase in the use of prescription opioids in the Bellwether communities that resulted from the Defendant manufacturers' promotion of prescription opioids since 1995?"[368]

(211) Professor Rosenthal answers this question by employing two types of regression models, which she refers to as direct and indirect models. Her direct model "quantif[ies] directly the causal relationship between promotion and sales" and her indirect model assesses "changes in demographic, economic and medical conditions as an additional approach that explains the growth in opioid sales from marketing and which avoids some measurement challenges inherent in the first [direct] approach."[369] Professor Rosenthal describes this latter model as an "indirect" method "in that the method permits an inference that a remaining mechanism, promotion, was causal."[370] Professor Rosenthal concludes as follows:

> Using econometric models, I demonstrate that I can reasonably identify the extent to which the sale of prescription opioids (measured by the number of milligrams of morphine equivalents, or MMEs) was caused by any quantum of the Defendants' promotional efforts that counsel can prove was unlawful. Based upon my analyses and assumptions from counsel about the extent of promotion that can be proven to be unlawful, I can reasonably identify approximately 45–67% of MMEs during the period of my analysis as caused by unlawful promotion.[371]

[368] Rosenthal Rep. ¶ 8.

[369] Rosenthal Rep. ¶ 10.

[370] Rosenthal Rep. ¶ 49.

[371] Rosenthal Rep. ¶ 11.

C.1.a. Professor Rosenthal's direct model

(212) Professor Rosenthal's direct model purports to measure the extent to which manufacturer promotional efforts, which she proxies using opioid detailing contact data from IQVIA's Integrated Promotional Service ("IPS") data, and a "class-wide price index for opioid drugs" explains the "number of MMEs for all drugs at issue in this matter…[a] measure of impact that is conceptually connected to the harms that are quantified in the report by Prof. David Cutler." As described below, Professor Rosenthal offers a version of her direct model (Model C) that "include[s] variables that capture some…key events."[372] Professor Rosenthal describes her rationale for using detailing contacts as the explanatory variable of interest:

> During at least the period relevant to this case (about 1995 to the present), pharmaceutical companies have employed a variety of promotional tactics for prescription drugs. These efforts may be directed at prescribers, patients or payers…Despite the numerous forms of pharmaceutical marketing, marketing to physicians and other professionals remains the largest component of pharmaceutical marketing. In total, marketing to physicians grew from $15.6 billion in 1997 to $20.3 billion in 2016 The 2016 figure includes $5.6 billion for detailing, $13.5 billion in free samples, and $979 million in "transfers of value" to physicians (e.g., speaking fees, meals) and $59 million for unbranded educational campaigns. Because of its economic importance as the leading category of promotional spending, promotion to physicians is the most studied form of pharmaceutical promotion. Thus, I devote special attention in this section to the role of promotion to physicians and its impact on prescribing.[373]

Professor Rosenthal opines that her direct model is conservative because it does not account for forms of promotion other than physician detailing:

> Note that in this case, there appears to be substantial evidence that through means other than promotional spending the Defendant manufacturers fundamentally changed opioid prescribing standards. The direct approach does not calculate the effects of the nonpromotional marketing, and is thus conservative. In short, I am confident in my direct-method estimates not only because of the relative importance of detailing, but also because detailing is often used in concert with other forms of promotion including samples and yields conservative results.[374]

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372 Rosenthal Rep. ¶ 60.

373 Rosenthal Rep. ¶¶ 23–24.

374 Rosenthal Rep. ¶ 56.

(213) Professor Rosenthal's physician detailing variable consists of a "stock" of detailing contacts that accumulate over time and depreciate at a rate that her model determines to best fit the pattern of opioid MMEs. She explains:

> Detailing contacts were entered into the model as a stock, including the number of current contacts and the depreciated value of past contacts, in line with the published literature and in accordance with the theory that effects of promotion on prescribing are dynamic. The stock of contacts in month t, S_t, was computed as follows:
>
> $S_t = Contacts_t + (1 - \delta)\, S_{t-1}$
>
> Where:
>
> $Contacts_t$ is the number of detailing contacts in month t, and
>
> S_{t-} is the depreciated value of past contacts.
>
> The parameter δ is the depreciation rate, which I estimate in the model along with the other parameters.[375]

Professor Rosenthal's direct models estimate a depreciation rate that indicates that promotion stock *grew* by 8.3% annually. She concedes that this negative depreciation is inconsistent with literature that finds that promotion stock decays over time, but provides the following rationale:

> The depreciation rate of -0.0067 translates to an annual rate of -8.3%. A negative depreciation rate indicates that the stock of promotion grows over time. While this prediction may be at odds with the usual marketing literature, it is perfectly consistent with an addictive product like opioids.[376]

(214) Professor Rosenthal offers three versions of her direct model. She describes each as follows:

- "Model A assumes that the effectiveness of detailing is constant over the period 1993–2018…Model A does not capture well either the initial growth in opioid sales or the change that occurred in 2011. In short, estimating Model A teaches us that there is likely a changing, not constant, relationship between detailing and sales over this long (1993–2018) time period that should be explored to more accurately describe the relationship."[377]
- "Model B allows the effectiveness of promotion to change at two points in time, determined using specification tests. Thus, this model captures three different periods or eras of the opioid market:

[375] Rosenthal Rep. ¶ 62.

[376] Rosenthal Rep. ¶ 72; *See also Rosenthal May 4 Dep. at 259:25–260:4.*

[377] Rosenthal Rep. ¶ 70.

the initial era, an increase in MME sales during the second era, and a third era marking the gradual decline in MME sales. Specifically, we allow for an additive shift in promotional effectiveness that occurs in April 2002 (which enters as the interaction between the stock of detailing and a dummy variable that is zero before and 1 after April 2002) and then with a secular decrease in promotional effectiveness that begins in September 2010 (which enters as the interaction between the stock of detailing and a linear trend that is zero before September 2010 and increments by month)."[378]

- In Model C, Professor Rosenthal "…tested the robustness of Model B by examining whether indicators of specific events and policies should be explicitly included in my model. To test for the impact of specific events on the empirical model, I introduced dummy variables" for the following events:
  - January 1998 Consensus Statement from American Academy of Pain Management ("AAPM") and the American Pain Society ("APS")
  - January 1999 Federation of State Medical Boards Model Guidelines
  - January 2001 JCAHO pain standards
  - August 2010 OxyContin reformulation
  - October 2014 rescheduling of hydrocodone from DEA schedule III to schedule II

  "These dummy variables are set to zero up to the month in which the event occurs and one thereafter…Model C uses the same turning points as used in Model B (i.e., April 2002 and September 2010)… Jointly, all five events are not statistically different from zero. It is also worth noting that the adjusted R-squared statistic (which adjusts for the number of additional variables included in the model) in Model C barely improves upon the adjusted R-squared in Model B and the main results concerning promotion and price are little changed."[379]

Professor Rosenthal prefers Model B of her direct approach. She explains:

> Given these results and applying accepted principles of econometrics, I am of the opinion that Model B is a fair, accurate and econometrically sound method by which to estimate the relationship of the Defendants' detailing of opioids on the sales of prescription opioids over the time period 1993 to 2018.[380]

[378] Rosenthal Rep. ¶ 71.

[379] Rosenthal Rep. ¶ 73, Table 1.

[380] Rosenthal Rep. ¶ 74.

(215) Using the results from Model B of her direct approach, Professor Rosenthal calculates the percentage difference between her predicated actual MMEs and MMEs that would result after removing the effect of unlawful promotion. She explains:

> I have been instructed by counsel to assume in my but-for scenarios that the fact finder (judge or jury) finds that all or virtually all promotion by the manufacturer Defendants from 1995 to the present was unlawful… I model a world in which this promotion did not occur (i.e., but-for promotion equals actual promotion for opioids less all promotion for opioids by the Defendants and their surrogates). To calculate the number of MMEs that would have been filled but-for the alleged wrongdoing, I replace actual detailing with but-for detailing and generate monthly predicted but-for MMEs…I then take the differences between predicted actual MMEs and the predicted MMEs that would have been prescribed and purchased under the assumption of the but-for scenario.[381]

Professor Rosenthal's but-for detailing consists of all detailing conducted by non-defendant manufacturers, and she predicts the effects of this non-defendant detailing using the same estimates applied to defendant detailing. Thus, Professor Rosenthal assumes that challenged and non-challenged promotion have the same effect. On average over the period from 1995–2018, Professor Rosenthal finds that 44.9% of MMEs were "attributable to challenged promotion." The percentage of MMEs attributable to challenged promotion increased over time, from 5.5% in 1995, to 33.4% in 2000, to 54.1% in 2010, and to 63.8% in 2018.[382]

(216) Professor Rosenthal evaluates the "sensitivity of [her] calculations of impact [from her direct model B] to the inclusion or exclusion of particular Defendants' promotional efforts in the construction of [her] but-for scenario."[383] Professor Rosenthal does not report a result of this sensitivity for Allergan, but she does include Allergan's products in the result that she reports for Actavis. As reflected in her Table C.3 and backup data, Professor Rosenthal's Actavis sensitivity accounts for detailing contacts associated with the following drugs: Anexsia, Combunox, Kadian, hydrocodone/APAP, hydrocodone/ibuprofen, Lorcet, Maxidone, meperidine, Norco, oxycodone, oxymorphone ER, Procet, and Reprexain. Allergan's two remaining opioid products are Kadian and Norco. I explain in Section II.B that I have been asked by counsel for Allergan to assume that for drugs other than Kadian and Norco, Allergan either does not own the liability for those products or those products are not the subject of any allegations of marketing misconduct in this case.

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381 Rosenthal Rep. ¶ 75.

382 Rosenthal Rep. Table 2.

383 Rosenthal Rep. ¶ 76.

C.1.b. Professor Rosenthal's indirect model

(217) Professor Rosenthal's indirect model attributes to manufacturer misconduct any opioid shipments (as recorded in DEA ARCOS data) not explained by certain demographic, economic, and medical conditions. Professor Rosenthal explains:

> In particular, we employ data at the county level where there is substantial geographic variation in demographic, economic, and health care characteristics and run the regression for a single cross-section in the "pre-misconduct" period (in fact, the earliest data we have is 1997 our results are likely conservative). This regression is then used to predict sales that would have been expected given only changes in economic, demographic, and health care factors. Similar to the but-for calculations of sales using the direct method, predictions from the indirect method represent an estimate of opioid sales in the absence of Defendants' misconduct.[384]

Professor Rosenthal includes the following demographic, economic, and health care variables in an attempt to explain the county-level variation in opioid shipments:[385]

- Demographic variables: "percent of the population that is male, the percent in different age groups (<15, 15–29, 30–44, 45–64, 65+), the percent of the population that is white, the percent that is black, the percent that is Hispanic, the share of the population in four different education groups (less than a high school degree, a high school degree, some college, and a college degree), and the percent of the county identified as urban."
- Economic variables: "unemployment rate and employment-to-population ratio; the distribution of employment by major industry sector; median household income ($000); the poverty rate; and the county's population."
- Health care variables: "the percentage of the population without insurance coverage; and the number of cancer deaths."

(218) Professor Rosenthal uses the "results of [her] regression model, together with data on explanatory variables for 1998–2016…to predict MMEs for the post-1997 period that would have been observed in the absence of Defendants' alleged misconduct." Professor Rosenthal accounts for "secular trends that are not captured by demographic, economic and health care variables" by adding to her "predicted MMEs an annual increased based on an estimated linear trend using…data from the International Narcotics Control Board" for the period from 1980–1995. Professor Rosenthal also "adjust[s] for the impact of aggregate prices for opioids:"

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384 Rosenthal Rep. ¶ 79.

385 Rosenthal Rep. ¶ 84.

> As the predicted effect of rising prices on but-for MMEs is negative, this adjustment reduces the but-for value and increases the estimated excess MMEs. But the relatively low elasticity of demand means the adjustment is small, reducing the excess share of total MMEs from the indirect model by an average of 0.5 percentage points per year.[386]

On average over the period from 1996–2016, Professor Rosenthal finds that 67% of opioid MMEs are unexplained by the demographic, economic, and medical variables she includes in her model, a residual that she attributes entirely to manufacturer misconduct.[387] She states:

> Actual opioid sales increased sharply after 1995 but projections from the indirect regression model indicate that opioid sales would have grown much more slowly in the absence of Defendants' actions.[388]

C.1.c. Professor Rosenthal's assessment of "under-treated" pain

(219) Professor Rosenthal also purports to "approximate the portion of the increased prescribing caused by the allegedly unlawful promotion could possibly be associated with using opioids to address ostensibly 'under-treated' pain."[389] To do so, Professor Rosenthal relies on the opinions of Plaintiffs' experts Dr. Schumacher and Dr. Parran. Professor Rosenthal calculates the number of patients treated nationally and in Cuyahoga and Summit counties for certain diagnoses, and multiplies that number by the daily dose in MMEs and the duration of treatment in days she claims are recommended for each diagnosis. Professor Rosenthal includes "cancer patients at the end of life/in hospice," and "patients who are treated for trauma and patients who undergo surgery."[390] Professor Rosenthal acknowledges the limitations of her approach:

> Given the narrow categories of indicated chronic pain use, its role as third-line therapy, and the significant risks associated with its use, optimal chronic opioid therapy is difficult to characterize even in this approximate way with a single regimen. For these reasons, I do not attempt to capture optimal treatment for patients with chronic pain in my simulation.[391]
>
> …

386 Rosenthal Rep. ¶ 88.

387 Rosenthal Rep. Table 5.

388 Rosenthal Rep. ¶ 89.

389 Rosenthal Rep. ¶ 91.

390 Rosenthal Rep. ¶¶ 95, 97.

391 Rosenthal Rep. ¶ 93.

> Note that because I am not documenting the diagnoses and dosing associated with actual uses of opioids, I am not able to calculate how much of the increased use of opioids during the period in which the alleged misconduct occurred was in fact for clinically appropriate indications, dosages, and durations.[392]

(220) Professor Rosenthal does not offer an opinion about whether Allergan's promotion was unlawful, nor does she separately assess the extent to which any Allergan promotion caused an increase in opioid prescribing or shipments.

C.2. Professor Cutler's estimation of the percentage of harms that is attributable to Defendants' alleged misconduct

C.2.a. Professor Cutler's estimation of the percentage of harms attributable to opioids

(221) Professor Cutler begins by "estimating the share of various harms attributable to opioids, including those related to both prescription opioids and illicit opioids," for five divisions of the Bellwether governments.[393] Specifically, Professor Cutler analyzes the following categories of harm:

> [C]riminal activity that imposes costs on Bellwether divisions that provide police and public safety services; the demand for services related to children and families that imposes costs on Bellwether divisions responsible for children and family services; the demand for addiction treatment services funded by Bellwether governments; and the demand for services by medical examiners (coroners), which are also provided by Bellwether governments.[394]

Professor Cutler describes this first step as including "multiple parts, and for several categories of harm requires estimating (i) the share of harms that are due to drug use in general (including both opioids and non-opioids) and (ii) the share of these drug-related harms that are attributable to opioids."[395] Professor Cutler's calculations for the five categories of harm can generally be performed using the following equation:

$$\text{Share of Harms Attributable to Opioids} = \text{Share of Harms Attributable to Drugs}$$

[392] Rosenthal Rep. ¶ 94. (emphasis removed).

[393] Cutler Rep. ¶ 24.

[394] Cutler Rep. ¶ 20.

[395] Cutler Rep. ¶ 24.

x Share of Drug Harms Attributable to Opioids[396]

As Professor Cutler notes in his report, "[i]n some instances, however, data are available that allow direct estimation of the percentage of harms due to opioids in a single calculation."[397]

(222) Professor Cutler relies on several data sources to perform his harm calculations, some of which are specific to the counties he is analyzing and some of which are national in scope. I address the details of these data sources, including why I believe some are inappropriate, in Section VI.G.

(223) To supplement this analysis, Professor Cutler also performs a "confirmatory analysis with regards to the effect of prescription opioid shipments on crime…using a direction regression approach."[398] Professor Cutler claims that, "the results of this analysis confirm the effect of defendants' shipments on crime estimated using [his] primary approach."[399]

(224) Specifically, Professor Cutler "estimates the effect of average shipments on [the change in] crime rates (which are calculated as the number of reported crime incidents per 100,000 population)," for three categories of crimes, "property crime (examples include burglary, larceny, and theft), violent crime (examples include murder and assault), and crimes against society (which includes drug crimes)."[400] In doing so, Professor Cutler uses "the same measure of shipments as used in the direct impact regression," as well as "additional control variables [including] economic and demographic factors whose effect on crime has previously been studied."[401]

(225) The results of Professor Cutler's crime regression analysis show that:

> [a]ll else equal, crime tends to be higher in areas with a larger population of younger people, men, and in areas where economic outcomes are worse. For both property and violent crime, the regressions show a positive and statistically significant relationship between opioid shipments to a county and the changes in the incidence of crime between 1995–96 and 2015–16. That is, all else equal, crime fell less in areas with larger opioid shipments, even when controlling for demographic and economic changes.[402]

396 Cutler Rep. ¶ 24.
397 Cutler Rep. ¶ 24.
398 Cutler Rep. ¶ 124.
399 Cutler Rep. ¶ 124.
400 Cutler Rep. ¶ 128–129.
401 Cutler Rep. ¶ 131–132.
402 Cutler Rep. ¶ 133.

Professor Cutler uses the shipments coefficient estimated by his model to estimate the effect of opioid shipments on crime rates and suggests that "the crime regression analysis confirms [his] earlier conclusions suggesting, if anything, that the results…are conservative."[403]

C.2.b. Professor Cutler's estimation of the share of opioid-related mortality attributable to opioid shipments

(226) Professor Cutler explains that, "because these jurisdictions would have faced some opioid-related costs even in the absence of the increasing availability of prescription opioids due to the defendants' misconduct, it is necessary to estimate the share of opioid-related harms that are attributable to shipments of prescription opioids."[404] Professor Cutler uses mortality data to perform this step of his analysis "because of the direct connection between availability of legal and illegal opioids and opioid-related deaths."[405] In fact, Professor Cutler states that, "there is no reason to expect there would be opioid-related deaths in the absence of supplies of prescription opioids and illegal substitutes."[406]

(227) Professor Cutler employs two types of regression models to analyze the relationship over time between prescription opioid shipments and mortality. Similar to Professor Rosenthal, Professor Cutler uses both a direct and an indirect regression model. Professor Cutler describes his direct model as "based on the relationship between changes over time in opioid mortality across different geographic areas and shipments of prescription opioids to those areas."[407] His indirect approach "uses the relationship between opioid mortality across areas and social and economic characteristics of those areas prior to defendants' misconduct to project changes in opioid-related mortality expected in the absence of excessive shipments of prescription opioids."[408]

(228) Professor Cutler claims that his statistical analysis "must recognize…the dramatic change in nature of the opioid crisis after 2010," a change that he describes in his report.[409] Both Professor Cutler and Professor Gruber identify that "there are distinct phases of the current opioid epidemic, with 2010 marking an approximate transition point for the beginning of the decline in overall prescriptions opioid shipments."[410] Due to this "dramatic change" in 2010, Professor Cutler claims that "it is

403 Cutler Rep. ¶ 133.
404 Cutler Rep. ¶ 47.
405 Cutler Rep. ¶ 47.
406 Cutler Rep. ¶ 47.
407 Cutler Rep. ¶ 48.
408 Cutler Rep. ¶ 48.
409 Cutler Rep. ¶ 64.
410 Cutler Rep. ¶ 50.

inappropriate to use a direct regression method to measure the effect of prescription opioids on opioid mortality after 2010.[411]

(229) Professor Cutler's direct model purports to analyze the "relationship between the increase in opioid-related mortality in a geographic area and per capita shipments of prescription opioids to that geographic area."[412] He notes that, "[b]ecause this specification cannot fully account for the transition from licit to illicit opioids after 2010, the change in mortality is evaluated based on the difference in average opioid-related mortality rates in an area between 1993–95 and 2009–10."[413] Professor Cutler concludes from his direct model that:

> All else equal, each unit increase in shipments between 1997 and 2010 (measured in MME per capita per day) raises the mortality rate by 4.39 deaths per 100,000… In summary, these results show that even with very extensive controls for economic and social factors, there remains a strong, statistically significant, and large relationship between prescription opioid shipments and opioid-related mortality through 2010.[414]

(230) In his direct model, Professor Cutler attempts to "control for other factors that might affect opioid mortality."[415] For example, he describes that,

> One variable included in the model is the area's opioid mortality rate in 1993–95. Inclusion of this variable is designed to capture any mean reversion in mortality rates. Such an effect occurs when, for example, areas with lower initial morality (sic) may have larger mortality increases simply because they are catching up to their peer areas (or vice-versa). Such 'mean reversion' would be expected if, for example, opioid mortality was unusually high or lower for reporting reasons in the initial period.[416]

The control variables that Professor Cutler uses in his regression model, including a number of demographic and economic characteristics which he believes may affect mortality, are measured in a similar way (i.e., the "model includes those levels as well as their changes over the time period"[417]). These demographic and economic characteristics include:

> The percent of the population that is male, the percent in different age groups (<15, 15–29, 30–44, 45–64, 65+), the percent of the population that is white, the percent

411 Cutler Rep. ¶ 68.
412 Cutler Rep. ¶ 65.
413 Cutler Rep. ¶ 82.
414 Cutler Rep. ¶ 92.
415 Cutler Rep. ¶ 86.
416 Cutler Rep. ¶ 86.
417 Cutler Rep. ¶ 88.

> that is black, the percent that is Hispanic, the share of the population in four different education groups (less than a high school degree, a high school degree only, some college, and a college degree or higher), and the percent of the county identified as urban.
>
> …
>
> The model includes the unemployment rate and employment-to-population ratio; the distribution of employment by major industry sector; median household income ($000); the poverty rate; and the county's population.[418]

(231) Professor Cutler's indirect regression model purports to estimate "the relationship between the opioid mortality rate in an area and the economic and demographic characteristics of the area."[419] He then uses the regression estimates "to project how opioid mortality would have changed in response to changes over time in the economic and demographic characteristics, but without misconduct on the part of the defendants."[420] In his indirect model, Professor Cutler again addresses the alleged change in environment beginning after 2010, stating that, "the indirect regression model for the post-2010 period is used to evaluate how deaths due to illicit opioids would have changed after 2010 in response to changes in economic and demographic factors in the absence of the increased demand for illicit opioids."[421]

(232) Professor Cutler's indirect "regression model explains variation across counties in the average death rate due to use of illicit opioids in 2008–2010," and "includes controls for county-specific demographic and economic characteristics," also measured from 2008–2010.[422] He then uses the results of his regression "together with data on explanatory variables for 2011–16…to predict 'but-for' mortality rates for illicit opioids for 2011–16 that would have been observed in the absence of the shift into illicit opioids after 2010 that resulted from earlier shipments of prescription opioids."[423] Professor Cutler claims that his results show that, "deaths due to illicit opioid use increased dramatically after 2010 but projections of the average but for illicit mortality rate based on the 2008–10 regression indicate that illicit mortality would have fallen in the absence of the decline in shipments of prescription opioids and the increased demand for illicit opioids after that time."[424]

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418 Cutler Rep. ¶ 88.
419 Cutler Rep. ¶ 93.
420 Cutler Rep. ¶ 93.
421 Cutler Rep. ¶ 94.
422 Cutler Rep. ¶ 94.
423 Cutler Rep. ¶ 97.
424 Cutler Rep. ¶ 97.

Professor Cutler suggests that this is because the overall economy was improving and therefore should have led to fewer deaths from illicit opioids.

(233) Professor Cutler estimates a second indirect model "to estimate the effect of prescription opioids on total opioid mortality over the entire 1995–2016 time period," using the same demographic and economic controls described above.[425] He uses the results of this regression to "predict mortality rates for the post-1995 period that would have been observed in the absence of the acceleration in prescription opioid shipments after 1995."[426] Professor Cutler concludes that "opioid mortality increased dramatically after 1995 but projections of the average 'but for' opioid related mortality on the 1993–95 indirect regression model indicate that opioid mortality generally would have been stable in the absence of defendants' actions."[427]

(234) After completing the steps of his analysis as described above, Professor Cutler purports to "[estimate] the impact on opioid-related mortality from prescription opioid shipments resulting from defendants' misconduct," which then becomes an input into Professor McGuire's analysis.[428] Professor Cutler describes that, "these calculations combine (i) estimates of the share of shipments of prescription opioids that are attributable to defendants' misconduct estimated by Prof. Rosenthal, with (ii) each of the two approaches to estimating the impact of shipments of prescription opioids on opioid-related mortality."[429]

(235) Professor Cutler utilizes two different approaches to estimate the "impact of defendants' misconduct on opioid mortality."[430] He describes his first approach as having three parts:

> 1. The share of opioid-related mortality from 2006 to 2010 that is attributable to defendants' misconduct is calculated using the results of the direct regression model and incorporating the estimates of the share of prescription opioid shipments due to defendants' misconduct calculated by Prof. Rosenthal;
>
> 2. The share of *licit* opioid-related mortality from 2011 to 2016 that is attributable to defendants' misconduct is calculated using the results of the direct regression model and incorporating the estimates of prescription opioid shipments due to defendants' misconduct calculated by Prof. Rosenthal; and

425 Cutler Rep. ¶ 98.
426 Cutler Rep. ¶ 100.
427 Cutler Rep. ¶ 100.
428 Cutler Rep. ¶ 101.
429 Cutler Rep. ¶ 101.
430 Cutler Rep. ¶ 102.

> 3. The share of deaths due to *illicit* opioids from 2011 to 2016 that is attributable to defendants' misconduct is calculated using an indirect regression model that estimates the increase in illicit opioid mortality that is unexplained by social and demographic factors relative to the pre-2011 baseline.[431]

Professor Cutler claims that his "results indicate that the share of opioid mortality attributable to [defendants'] misconduct grew from roughly 21 percent in 2006 to more than 47 percent by 2016."[432]

(236) According to Professor Cutler's report, "Approach 2 calculates the share of opioid mortality due to defendants' shipments attributable to misconduct based on the indirect regression model that estimates the relationship between opioid mortality and the economic and demographic characteristics of counties over the 1993–95 time period."[433] Professor Cutler claims that the "application of the indirect approach based on the 1993–95 benchmark reflects the view that increases in opioid mortality not attributable to changes in economic and demographic factors can be attributed to the growth in shipments of prescription opioids."[434] The results of Professor Cutler's Approach 2 indicate that the share of opioid mortality attributable to defendants' misconduct grew from roughly 36 percent in 2006 to more than 48 percent by 2016.[435]

(237) Professor Cutler provides an alternative analysis that "incorporates an estimate of the share of prescription opioids that should have been identified as suspicious by distributors."[436] He claims that, "some portion of the harm resulting from such shipments also could have been avoided has CSA registrants, such as defendant distributors, not acted improperly," and that this portion can be estimated.[437]

(238) Professor Cutler describes that, "the share of harm potentially attributable to distributors can be calculated by applying an estimate of the *share of excessive shipments that distributors failed to identify* (to the extent such a measure is available) instead of the estimate of the *share of shipments due to misleading marketing misconduct*."[438] Specifically, Professor Cutler adjusts his calculation as follows:

> Share of Harms Attributable to **Distributor** Misconduct
> = Share of Harms Attributable to Opioids
> x Share of Opioid Harms Attributable to Opioid Shipments

[431] Cutler Rep. ¶ 102.
[432] Cutler Rep. ¶ 115.
[433] Cutler Rep. ¶ 116.
[434] Cutler Rep. ¶ 116.
[435] Cutler Rep. Table III.14.
[436] Cutler Rep. ¶ 9.
[437] Cutler Rep. Appendix III.J, ¶ 2.
[438] Cutler Rep. Appendix III.J, ¶ 4.

x Share of Opioid Shipments Due to **Distributor** Misconduct[439]

Professor Cutler calculates this estimate using "data on the share of shipments for which the distributors are liable that [were] provided to [him] by counsel," and presents his results in Appendix III.J.[440]

(239) Finally, Professor Cutler combines these steps to estimate "the share of the various harms…that result from shipments of prescription opioids that are attributable to defendants' misconduct."[441] Professor Cutler performs this calculation as:

Share of Harms Attributable to Defendants' Misconduct
= Share of Harms Attributable to Opioids
x Share of Opioid Harms Attributable to Opioid Shipments
x Share of Opioid Shipments Due to Defendants' Misconduct[442]

The results of this calculation can be found in Professor Cutler's Tables III.16A and III.16B.[443]

C.3. Professor McGuire's analysis

(240) Professor McGuire was asked by counsel to determine if "there is a valid economic methodology for attributing a share of Bellwether government costs to defendants' misconduct," and "if a valid framework for assigning a share of Bellwether government costs to damages does exist…[to calculate] the amount of those damages, both in total and broken out by each Bellwether government and by budgetary components starting in 2006 and continuing through 2018."[444] Professor McGuire handles this assignment in his damages report. Separately, Professor Cutler was asked by counsel to opine on "whether there is a public nuisance that resulted from the shipment of prescription opioid products into the Bellwether communities over the period 2006 to the present that has impacted those communities," and if so what is "the magnitude of the economic costs imposed on the Bellwether communities over the period 2006 to 2016…taking into account any potential economic benefits with respect to the shipments."[445] Professor McGuire handles this assignment in his Public Nuisance report.

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439 Cutler Rep. Appendix III.J, ¶ 4 (emphasis in original).

440 Cutler Rep. Appendix III.J, ¶ 6.

441 Cutler Rep. ¶ 118.

442 Cutler Rep., ¶ 23.

443 Cutler Rep. Table III.16A, Table III.16B.

444 McGuire Damages Rep. ¶ 7.

445 Expert Report of Professor Thomas McGuire Regarding Public Nuisance, March 25, 2019 [hereinafter "McGuire Nuisance Rep."] ¶ 6.

C.3.a. Professor McGuire's damages framework

(241) Professor McGuire identified a damages framework that he describes as being

> based on a straightforward chain of reasoning that links (i) misrepresentations by manufacturer defendants and failure to detect and prevent excessive opioid shipments by all registrants of the Controlled Substances Act ("CSA"), including the distributor defendants, to greater shipments of prescription opioids; (ii) increase in prescription opioid shipments to increases in harms (e.g., crime, overdoses) in the Bellwether jurisdictions; and (iii) increases in harms to costs faced by Bellwether governments which devoted resources to contend with these harms.[446]

More specifically Professor McGuire estimates damages "by applying the estimates of the percent of harms attributable to defendants' misconduct presented in the Cutler Report…to the identified affected costs in each division,"[447] and claims that his analysis "addresses how the increased demand for services resulting from defendants' misconduct translates into damages to Bellwether divisions."[448]

(242) In order to perform his analysis, Professor McGuire must first identify the divisions of the Bellwether Governments that were affected by the opioid abuse crisis. Professor McGuire claims that "an argument can be made that, to at least some extent, all municipal government division have been impacted by the opioid crisis," however his analysis, "is confined to certain divisions that are more likely to have been most affected and are therefore likely to have incurred the largest costs."[449] To identify these divisions, Professor McGuire and his team "reviewed budget and expenditure information from the Bellwether governments," and, "reviewed the activities undertaken by each of the larger divisions to determine whether these divisions were likely to have been affected in line with …the effect the opioid epidemic has had on the demand for certain services provided by the Bellwether governments."[450] Overall, Professor McGuire identified nine divisions of Cuyahoga County and ten divisions of Summit County that "provide services generally related to (1) criminal activities occurring in the area (e.g. courts and adjudication, medical examination, and prisons); (2) child services (e.g., Children and Family Services); or (3) public health initiatives (e.g. ADAMHS/ADM boards)," which have been impacted by the opioid abuse crisis.[451]

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[446] McGuire Damages Rep. ¶8.

[447] McGuire Damages Rep. ¶11.

[448] McGuire Damages Rep. ¶16.

[449] McGuire Damages Rep. ¶40.

[450] McGuire Damages Rep. ¶51.

[451] McGuire Damages Rep. ¶51–54.

(243) The next step in Professor McGuire's analysis is to identify the affects costs within each impacted government division. To do so, Professor McGuire "reviewed each cost category (e.g., wages and salaries, supply purchases) for the relevant divisions identified," using "the expenditure data of the Bellwether governments."[452] He then identifies "those costs that would be expected to vary in response to changes in the services provided by these divisions," focusing on the largest line items per division.[453] Finally, Professor McGuire estimates "how much of these costs in each category were incurred in providing activities or services affected by the opioid crisis."[454] This step "requires excluding estimates of costs related to staff in overhead or support activities (e.g. IT services or accounting) that were unlikely to have been affected by the crisis," as well as other adjustments to exclude costs that were "unlikely to have been affected by the opioid crisis."[455]

(244) Professor McGuire uses the calculation above to identify the "share of total costs in relevant divisions that address harms."[456] He then multiplies that share by "the total costs faced by Bellwether divisions affected by the opioid crisis," and the "share of harms attributable to defendants' misconduct," which he gets from Professor Cutler, in order to estimate damages.[457]

C.3.b. Professor McGuire's public nuisance opinions

(245) For his public nuisance analysis, Professor McGuire relies on "the following general definition of a public nuisance:

> The definition of 'public nuisance'…is couched in broad language. According to the Restatement [(Second) of Torts], a 'public nuisance' is 'an unreasonable interference with a right common to the general public."…'Unreasonable interference' includes those acts that significantly interfere with public health, safety, peace, comfort, or convenience, conduct that is contrary to a statute, ordinance, or regulation, or conduct that is of a continuing nature or one which has produced a permanent or long-lasting effect upon the public right, an effect of which the actor is aware of should be aware."[458]

(246) Professor McGuire's analysis of the alleged public nuisance created by Defendants' follows three steps. First, Professor McGuire reviews the relationship between public nuisance and externalities, which includes "a discussion of the nature of negative externalities associated with shipments of

[452] McGuire Damages Rep. ¶58.
[453] McGuire Damages Rep. ¶59.
[454] McGuire Damages Rep. ¶60.
[455] McGuire Damages Rep. ¶60.
[456] McGuire Damages Rep. ¶72.
[457] McGuire Damages Rep. ¶72.
[458] McGuire Nuisance Rep. ¶ 7.

prescription opioids, the role of the presence of positive effects of opioid use, and example of public response to negative externalities."[459] Next, Professor McGuire identifies "a series of harms caused by opioid shipments and quantify them for the Bellwether communities" and then purports to monetize those harms.[460]

(247) Professor McGuire states that, "the legal concept of a public nuisance parallels the concept of a negative externality in economics. An externality is created when a private actor harms others and does not compensate others for those effects. If the negative externality satisfies the other components of the definition mentioned earlier, it qualifies as a public nuisance."[461] He goes on to claim that,

> the ultimate 'consumers' of prescription opioids (patients) were not properly informed about the risk of harms associated with prescription opioids because their doctors were systematically misled by manufacturers. Without full knowledge of harms, a consumer cannot take them into account, nor can the consumer weigh the harms and costs relative to any purported benefits.[462]

Professor McGuire does, however, note that "a comprehensive evaluation of a public nuisance from an economic perspective considers both the positive and negative effects of the potential public nuisance," and purports to consider both costs and benefits in his analysis.[463] Professor McGuire concludes that:

> 1. Shipments significantly interfered with public health, safety, peace and comfort of members of the Bellwether communities with continuing and long-lasting effects.
>
> 2. The interference from shipments was unreasonable; and
>
> 3. Defendants were or should have been aware of the interference.[464]

In particular, Professor McGuire cites the high opioid mortality rates in both Summit and Cuyahoga counties, along with morbidity, crime, child maltreatment, and neonatal abstinence syndrome as establishing the "existence of significant long-term negative effects of shipments on the public health, safety and peace of members of the Bellwether communities.[465]

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459 McGuire Nuisance Rep. ¶ 11.
460 McGuire Nuisance Rep. ¶ 11.
461 McGuire Nuisance Rep. ¶ 18.
462 McGuire Nuisance Rep. ¶ 22.
463 McGuire Nuisance Rep. ¶ 24.
464 McGuire Nuisance Rep. ¶ 38.
465 McGuire Nuisance Rep. ¶ 42.

(248) After having established the long-term negative effects, Professor McGuire considers "whether the shipments of prescription opioids were reasonable or unreasonable from two perspectives. The first perspective considers whether the shipments were reasonable from the standpoint of being used for clinically justified treatment. The second perspective considers whether the shipments were reasonable from the standpoint of economic costs and benefits."[466] He relies on Professors Rosenthal and Gruber, as well as Dr. Schumacher, to establish that "the vast majority – at least 80% in Cuyahoga and at least 90% in Summit – of shipments to the Bellwether communities over this period were not justified by clinical need and were therefore unreasonable."[467]

(249) To analyze the benefits and costs of opioid use, Professor McGuire considers workforce participation and productivity as well as quality of life. He concludes that, "positive productivity and quality-of-life effects of scientifically acceptable pain treatment are vastly outweighed by the negative effects on productivity and quality of life. The net social contribution of shipments of prescription opioids is negative and large."[468] Furthermore, Professor McGuire claims, "Defendants had clear knowledge that the shipments had negative impacts on the public health and safety of communities across the nation, including in the Bellwether communities."[469] Based on the criteria laid out above, Professor McGuire concludes, "Defendants' shipment and distribution of prescription opioids constituted a public nuisance."[470]

(250) The final step of Professor McGuire's public nuisance analysis is to "put dollar values on the deaths, cases of OUD, babies born with NAS, crimes, and child maltreatment attributable to shipments."[471] He does so using multiple methods and sources to value these categories of harms, which are outlined in Figure 54.

[466] McGuire Nuisance Rep. ¶ 61.

[467] McGuire Nuisance Rep. ¶ 70.

[468] McGuire Nuisance Rep. ¶ 89.

[469] McGuire Nuisance Rep. ¶ 91.

[470] McGuire Nuisance Rep. ¶ 97.

[471] McGuire Nuisance Rep. ¶ 111.

Figure 54: Categories of Harms Due to Shipments and Method of Valuation

Form of Harm	Method Used for Valuation	Primary Sources for Valuation
Mortality: Deaths	Value of statistical life (VSL)	U.S. Health and Human Services guidance
Morbidity: OUD Cases	Elevated health care costs	Review of relevant literature
Babies with NAS	Elevated health care costs	Review of relevant literature
Crimes	Valuation	Review of relevant literature
Child Maltreatment	Elevated costs	Review of relevant literature
Bellwether Government Costs	Elevated costs	McGuire Report on Damages

Source: McGuire Nuisance Rep. Table 4.

Using these methods and sources, Professor McGuire concludes, "over the 11-year period, shipments of prescription opioids imposed net economic costs on the Bellwether communities of approximately $13.6 billion in Cuyahoga and approximately $6.5 billion for Summit."[472]

C.4. Professor Gruber's qualitative analysis

(251) Professor Gruber has been asked by counsel for the Plaintiffs to "provide, from the perspective of accepted principles of economics, an overview of the nation's opioid crisis."[473] He was also asked to opine on "whether, to a reasonable degree of certainty in the field of economics, the defendants' shipments of prescription opioids contributed, in whole or part, to the growth in the misuse of opioids and the increases in licit and illicit opioid-related mortality over the past 20 years."[474]

C.4.a. Professor Gruber's empirical overview of the opioid abuse crisis

(252) Professor Gruber begins his report with an overview of the opioid abuse crisis. In this overview, he reviews opioid use and trends in the time period before 1995, before transitioning to review the growth in shipments since 1995. Specifically, Professor Gruber claims that, "efforts to promote use of opioids in pain management accelerated with the launch of OxyContin in 1995."[475] He also claims that, "this period of promotional increase was associated with dramatic growth in the shipments of prescription opioids."[476] Professor Gruber then shifts his focus to describe the growth in opioid misuse after 1995, where he claims that, "the rapid growth in shipments of prescription opioids was

[472] McGuire Nuisance Rep. ¶ 135.

[473] Gruber Rep. ¶ 15.

[474] Gruber Rep. ¶ 15.

[475] Gruber Rep. ¶ 25.

[476] Gruber Rep. ¶ 27.

followed by a growth in opioid misuse and dependency."[477] Finally, Professor Gruber what he refers to as the "emergence of the illicit opioid crisis," which he describes as follows:

> Beginning around 2010, increased enforcement actions by DEA and DOJ, criminal actions and litigation, the growth of state PDMP laws, and increased awareness of addiction risks associated with prescription opioids contributed to a reduction in aggregate shipments of prescription opioids after more than 20 years of rapid growth.[478]

(253) Professor Gruber claims that "the substitution of illicit opioids for prescription opioids expanded dramatically starting around 2010, closely coinciding with the declines in shipments associated with increased legal enforcement, increased awareness of the potential for abuse, and the launch of abuse deterrent formulations."[479] Professor Gruber goes on to describe the increased use of heroin and fentanyl specifically before analyzing the impact of the opioid abuse crisis on the two Bellwether counties.

C.4.b. Professor Gruber's discussion of the impact of shipments on opioid dependence

(254) Professor Gruber purports to, "show that the increases in shipments of prescription opioids was a direct and substantial cause of the rapid growth in mortality from both licit and illicit opioid-related mortality in the past 20 years."[480] Specifically, Professor Gruber claims that, "the extreme variation in per capital shipments across areas suggests that prescription activity, which drives shipments to an area, bears little relationship to medical need,"[481] and that the "differences in the demographic and economic characteristics of counties explain very little of the observed differences in per capita shipments."[482]

(255) Professor Gruber tests this claim by evaluating, "the extent to which variation in per capita shipments can be explained by such [demographic and economic] factors," using regression analysis.[483] Professor Gruber concludes from this analysis that "the variation in the adjusted rates is only marginally smaller than that of the unadjusted rates, indicating that economic and demographic differences across counties explain little of the variation in per capita shipments across counties."[484]

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477 Gruber Rep. ¶ 29.
478 Gruber Rep ¶ 46.
479 Gruber Rep. ¶ 51.
480 Gruber Rep. ¶ 72.
481 Gruber Rep. ¶ 74.
482 Gruber Rep. ¶ 74.
483 Gruber Rep. ¶ 75.
484 Gruber Rep. ¶ 76.

In fact, Professor Gruber purports that his results imply that, "the wide variation in daily per capita MMEs across counties after controlling for differences in demographic and economic characteristics indicates that many shipments were excessive and unnecessary."[485]

(256) Professor Gruber also investigates "whether areas that received more shipments of prescription opioids have higher rates of growth of opioid mortality."[486] He does so by comparing "alternative measures of opioid mortality rates across counties with the highest per capita shipments between 1997–2010 that account for 25 percent of the population and those with the lowest shipments that account for 25 percent of the population."[487] Qualitatively, Professor Gruber concludes that this analysis shows that, "the growth in mortality, including that from prescription and illicit opioids, has a strong relationship with per capita shipments of prescription opioids between 1997–2010, with counties that received more shipments experiencing higher mortality rates," and points to Professor Cutler's report for the supporting statistical analysis.[488]

C.4.c. Additional evidence that the opioid abuse crisis was caused by shipments

(257) Professor Gruber also "reviews additional evidence establishing that the illicit opioid crisis would not have emerged in the absence of the prior increase in shipments of prescription opioids."[489] This evidence includes "epidemiological studies [that] establish the link between prescription opioids and heroin use,"[490] and "economic studies [that] have previously established the causal relationship between the increase in heroin-related mortality between 2010 and either 2012 or 2013 and defendants' earlier shipments of prescription opioids, as well as the reduction in sales after 2010."[491]

(258) Additionally, Professor Gruber "evaluates the effect of changes in economic, demographic and social conditions on opioid mortality and establishes that these factors cannot explain the emergence of the illicit opioid crisis in the absence of the prior increase in shipments of prescription opioids."[492] He does so using a two-step process which he describes as follows:

> First, I compare trends in opioid mortality in areas with different levels of economic activity in order to evaluate the extent to which opioid mortality trends are related to

485 Gruber Rep. ¶ 77.
486 Gruber Rep. ¶ 82.
487 Gruber Rep. ¶ 84.
488 Gruber Rep. ¶ 87.
489 Gruber Rep. ¶ 88.
490 Gruber Rep. ¶ 89.
491 Gruber Rep. ¶ 95.
492 Gruber Rep. ¶ 100.

economic opportunity. Second, I analyze the extent to which increases in opioid mortality are part of a larger trend in drug overdoses.[493]

(259) Professor Gruber concludes that these analyses "indicate that the increase in opioid-related mortality in both the U.S. and the Bellwether communities cannot be attributed to a more widespread increase in drug mortality," and that "the shipments of prescription opioids allowed these [economic] factors to be translated into opioid-related mortality and related harms."[494]

C.4.d. Shipments of prescription opioids are associated with higher crime

(260) Similar to Professor Cutler, Professor Gruber, "reviews evidence of the link between shipments of prescription opioids and higher levels of crime."[495] Specifically, Professor Gruber "documents the relationship between shipments of prescription opioids and crime using the FBI's UCR database."[496]

(261) In order to account for "the need to disentangle large and widespread declines in both property and violent crimes observed over recent decades," Professor Gruber "evaluate[s] the effects of shipments of prescription opioids on crime…separately for counties with high and low crime rates in 1995. Using this method, [Professor Gruber] evaluate[s] whether counties that received more shipments between 1997–2010 experienced lower declines in crime than low shipment counties."[497] Professor Gruber concludes that, "areas with higher shipments generally saw a smaller decline in crime than those areas with lower shipments, after controlling for initial crime rates," and refers to Professor Cutler's report for the supporting statistical analysis.[498]

493 Gruber Rep. ¶ 100.

494 Gruber Rep. ¶ 107.

495 Gruber Rep. ¶ 108.

496 Gruber Rep. ¶ 109.

497 Gruber Rep. ¶ 110–111.

498 Gruber Rep. ¶ 112.

Appendix D. Alternate sensitivities of Rosenthal models

Figure 55: Summary of fixed 0% depreciation model

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	6,805,905,942	***	-6,267,441,745	***	-2,180,023,774	***
b	Stock of Promotion	2,856	***				
b1	Stock of Promotion*Regime Dummy until Mar2002			1,485	***	2,476	***
b2	Stock of Promotion*Dummy from Mar2002			1,967	***	2,831	***
b3	Stock of Promotion*Dummy Trend from Aug2010			-15	***	-18	***
evt1	Consensus Statement From AAPM/APS 01/1998					-1,837,512,978	***
evt2	Federation of State Medical Boards Guidelines 01/1999					-370,851,352	
evt3	JCAHO pain standards releases 01/2001					-1,502,306,518	***
evt4	OxyContin Reformulation 08/2010					1,658,631,643	***
evt5	Hydrocodone Rescheduling 10/2014					699,032,536	**
main0	Fisher Ideal Price Index	-8,612,518,492	***	5,282,081,858	***	912,934,732	
RSquare		0.8805		0.9681		0.9831	
AdjRSq		0.8793		0.9673		0.9824	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 56: Overall percentage impact of Defendant promotion on MMEs, fixed 0% depreciation model

Year	Model A	Model B	Model C
1995	21.1%	14.7%	13.6%
1996	35.3%	28.5%	26.9%
1997	44.1%	29.3%	31.4%
1998	48.4%	30.9%	58.3%
1999	50.7%	37.0%	65.3%
2000	57.8%	42.3%	67.3%
2001	64.7%	46.5%	92.2%
2002	71.0%	49.8%	83.7%
2003	76.9%	51.9%	82.7%
2004	83.1%	51.4%	81.3%
2005	83.3%	52.6%	80.5%
2006	76.9%	56.8%	81.3%
2007	83.5%	54.5%	80.2%
2008	84.6%	54.2%	79.0%
2009	87.6%	53.2%	78.0%
2010	88.8%	52.8%	74.1%
2011	89.3%	51.7%	69.6%
2012	92.0%	49.0%	68.8%
2013	97.6%	46.3%	69.2%
2014	100.0%	42.4%	69.2%
2015	100.0%	39.9%	67.9%
2016	100.0%	37.3%	68.3%
2017	100.0%	34.6%	69.1%
2018	100.0%	30.7%	69.5%
TOTAL	**75.9%**	**43.6%**	**67.8%**

Source: Rosenthal backup data.

Figure 57: Summary of fixed 5% depreciation model

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	-10,766,196,425	***	-19,791,807,131	***	-9,196,715,110	***
b	Stock of Promotion	8,088	***				
b1	Stock of Promotion*Regime Dummy until Mar2002			1,937	**	-6,503	***
b2	Stock of Promotion*Dummy from Mar2002			8,291	***	-3,402	***
b3	Stock of Promotion*Dummy Trend from Aug2010			-345	***	-249	***
evt1	Consensus Statement From AAPM/APS 01/1998					1,592,356,249	***
evt2	Federation of State Medical Boards Guidelines 01/1999					2,115,539,333	***
evt3	JCAHO pain standards releases 01/2001					1,658,973,414	***
evt4	OxyContin Reformulation 08/2010					5,687,141,426	***
evt5	Hydrocodone Rescheduling 10/2014					-5,237,950,149	***
main0	Fisher Ideal Price Index	10,343,610,515	***	19,513,978,805	***	13,089,648,356	***
RSquare		0.6071		0.8642		0.9289	
AdjRSq		0.6031		0.8610		0.9260	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 58: Overall percentage impact of Defendant promotion on MMEs, fixed 5% depreciation model

Year	Model A	Model B	Model C
1995	14.5%	11.7%	-98.8%
1996	31.3%	25.1%	-158.5%
1997	33.5%	16.9%	-111.9%
1998	35.1%	15.7%	-64.2%
1999	44.3%	21.6%	-55.0%
2000	52.7%	24.3%	-76.6%
2001	57.6%	24.4%	-64.0%
2002	59.9%	44.6%	-30.7%
2003	58.3%	45.7%	-21.8%
2004	49.6%	36.8%	-17.3%
2005	46.8%	34.3%	-15.8%
2006	52.2%	39.3%	-15.4%
2007	40.6%	28.3%	-11.0%
2008	35.6%	24.3%	-9.7%
2009	30.5%	20.2%	-8.2%
2010	30.7%	19.8%	-8.8%
2011	31.0%	13.3%	-16.8%
2012	28.6%	0.5%	-30.5%
2013	26.7%	-14.3%	-39.4%
2014	23.8%	-26.4%	-48.5%
2015	21.2%	-35.9%	-62.7%
2016	17.2%	-40.3%	-56.4%
2017	14.2%	-43.6%	-51.1%
2018	10.9%	-33.0%	-36.1%
TOTAL	**35.9%**	**11.6%**	**-46.5%**

Source: Rosenthal backup data.

Figure 59: Summary of fixed 20% depreciation model

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	-10,811,971,873	***	-11,428,081,287	***	-5,839,796,336	***
b	Stock of Promotion	22,915	***				
b1	Stock of Promotion*Regime Dummy until Mar2002			2,229		-17,184	***
b2	Stock of Promotion*Dummy from Mar2002			39,109	***	3,100	
b3	Stock of Promotion*Dummy Trend from Aug2010			-815	***	-576	***
evt1	Consensus Statement From AAPM/APS 01/1998					1,254,705,999	**
evt2	Federation of State Medical Boards Guidelines 01/1999					1,795,333,665	***
evt3	JCAHO pain standards releases 01/2001					1,145,442,860	*
evt4	OxyContin Reformulation 08/2010					4,227,545,019	***
evt5	Hydrocodone Rescheduling 10/2014					-5,809,905,908	***
main0	Fisher Ideal Price Index	11,349,719,852	***	12,652,250,291	***	9,516,159,800	***
RSquare		0.5952		0.8561		0.9085	
AdjRSq		0.5911		0.8527		0.9047	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 60: Overall percentage impact of Defendant promotion on MMEs, fixed 20% depreciation model

Year	Model A	Model B	Model C
1995	22.4%	4.9%	-55.1%
1996	31.7%	6.4%	-56.4%
1997	25.1%	4.7%	-52.3%
1998	26.7%	5.2%	-46.5%
1999	36.5%	7.5%	-41.4%
2000	43.1%	8.9%	-56.3%
2001	44.0%	8.4%	-44.5%
2002	44.0%	41.6%	-3.0%
2003	38.1%	42.8%	3.7%
2004	28.2%	33.0%	2.8%
2005	28.1%	32.8%	2.8%
2006	27.8%	32.2%	2.2%
2007	20.7%	25.2%	1.8%
2008	19.1%	23.2%	1.8%
2009	16.1%	20.2%	1.5%
2010	20.6%	24.8%	1.5%
2011	20.4%	21.3%	-2.5%
2012	18.5%	15.2%	-7.8%
2013	16.8%	7.7%	-11.1%
2014	14.3%	0.2%	-15.9%
2015	10.3%	-4.6%	-18.0%
2016	6.7%	-6.5%	-14.2%
2017	5.2%	-7.8%	-12.7%
2018	2.7%	-4.4%	-6.0%
TOTAL	**24.2%**	**14.8%**	**-18.0%**

Source: Rosenthal backup data.

Figure 61: Summary of fixed 40% depreciation model

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	-10,854,500,574	***	-9,084,711,488	***	-6,015,629,857	***
b	Stock of Promotion	43,262	***				
b1	Stock of Promotion*Regime Dummy until Mar2002			-1,496		-25,563	***
b2	Stock of Promotion*Dummy from Mar2002			75,216	***	17,624	***
b3	Stock of Promotion*Dummy Trend from Aug2010			-1,270	***	-841	***
evt1	Consensus Statement From AAPM/APS 01/1998					1,089,855,243	*
evt2	Federation of State Medical Boards Guidelines 01/1999					1,697,760,389	**
evt3	JCAHO pain standards releases 01/2001					1,226,855,396	*
evt4	OxyContin Reformulation 08/2010					3,175,237,704	***
evt5	Hydrocodone Rescheduling 10/2014					-5,535,450,136	***
main0	Fisher Ideal Price Index	11,520,730,223	***	11,054,506,692	***	9,111,063,978	***
RSquare		0.5959		0.8544		0.9047	
AdjRSq		0.5918		0.8509		0.9008	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 62: Overall percentage impact of Defendant promotion on MMEs, fixed 40% depreciation model

Year	Model A	Model B	Model C
1995	20.8%	-1.4%	-34.6%
1996	22.7%	-1.4%	-32.5%
1997	17.7%	-1.1%	-30.3%
1998	20.3%	-1.4%	-27.7%
1999	27.7%	-2.0%	-24.9%
2000	32.2%	-2.4%	-32.6%
2001	31.8%	-2.2%	-23.9%
2002	32.0%	29.1%	4.1%
2003	26.5%	29.9%	7.5%
2004	19.3%	23.2%	5.6%
2005	20.4%	24.4%	6.1%
2006	17.9%	21.0%	4.2%
2007	14.6%	18.3%	3.9%
2008	13.4%	16.8%	3.8%
2009	11.4%	14.8%	3.3%
2010	15.6%	19.6%	4.5%
2011	14.3%	16.1%	2.1%
2012	13.2%	12.8%	-0.5%
2013	12.0%	8.5%	-2.9%
2014	10.1%	3.8%	-5.5%
2015	6.4%	0.1%	-6.0%
2016	4.4%	-1.8%	-5.5%
2017	3.4%	-2.8%	-5.1%
2018	1.2%	-1.3%	-1.8%
TOTAL	**17.4%**	**9.4%**	**-8.0%**

Source: Rosenthal backup data.

Figure 63: Summary of altered price index model

Parameter	Label	Model A		Model B		Model C	
		Estimate	Sig.	Estimate	Sig.	Estimate	Sig.
a	Constant	-1,667,020,307		41,485,192		-7,603,869	
b	Stock of Promotion	2,932	***				
b1	Stock of Promotion*Regime Dummy until Mar2002			981	***	1,023	***
b2	Stock of Promotion*Dummy from Mar2002			1,149	***	1,195	***
b3	Stock of Promotion*Dummy Trend from Aug2010			-9	***	-9	***
evt1	Consensus Statement From AAPM/APS 01/1998					-354,169,692	*
evt2	Federation of State Medical Boards Guidelines 01/1999					395,440,224	**
evt3	JCAHO pain standards releases 01/2001					-236,323,331	
evt4	OxyContin Reformulation 08/2010					33,803,132	
evt5	Hydrocodone Rescheduling 10/2014					296,642,800	
main0	Fisher Ideal Price Index (MMEs)	-333,433,557		257,408,187		282,441,066	
x	Depreciation constant	0.0035	***	-0.0061	***	-0.0059	***
RSquare		0.8563		0.9930		0.9932	
AdjRSq		0.8544		0.9928		0.9929	

Source: Rosenthal backup data. *** indicates 1%; ** indicates 5% significance; * indicates 10% significance.

Figure 64: Overall percentage impact of Defendant promotion on MMEs, altered price index model

Year	Model A	Model B	Model C
1995	22.7%	5.8%	5.9%
1996	35.7%	14.5%	14.9%
1997	39.4%	19.6%	19.9%
1998	41.9%	23.7%	27.2%
1999	46.9%	29.0%	29.1%
2000	53.6%	34.6%	34.8%
2001	59.7%	39.5%	41.4%
2002	64.6%	43.7%	45.4%
2003	68.3%	46.7%	48.3%
2004	69.7%	48.4%	49.9%
2005	70.5%	49.8%	51.2%
2006	71.6%	51.0%	52.3%
2007	72.1%	51.6%	52.8%
2008	72.1%	52.1%	53.2%
2009	72.0%	52.4%	53.5%
2010	71.9%	52.8%	53.8%
2011	71.0%	53.2%	54.1%
2012	69.5%	53.3%	54.2%
2013	70.1%	53.7%	54.6%
2014	71.3%	54.3%	54.9%
2015	71.9%	54.6%	54.6%
2016	71.4%	54.6%	54.5%
2017	70.8%	54.5%	54.4%
2018	70.5%	54.4%	54.2%
TOTAL	**62.3%**	**43.4%**	**44.3%**

Source: Rosenthal backup data.